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THE SURGICAL TREATMENT OF HÆMORRHOIDS *

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IT may be thought presumptuous to write about an affliction which has beset man since the dawn of history and which to-day is of such universal distribution that all who practise surgery must surely be well acquainted with its problems. The writer must therefore justify the contribution of another article upon this subject.

The results of any one of the many operations for hæmorrhoids are good; permanent anal stenosis is rare and recurrence of symptoms is uncommon enough to be accepted as a limitation inherent in any technical procedure. It is not the results of treatment which give cause for investigation but the path followed in achieving these results. If the patient suffers considerable pain for several days after operation, or requires instrumental dilatation of the anal canal for several weeks, the method employed is imperfect and a fit subject for criticism. Few articles give details of the post-operative progress of the patient and seldom contain any report of continued observation after the patient has left hospital. Despite statements that attention to detail in following a certain technique will eliminate pain it is common knowledge that in most cases these operations are extremely painful. This fact is well known to the general public and patients will often conceal rectal bleeding because of their dread of an operation. Were it possible to diminish this pain it is likely that the patients would more willingly seek advice about their symptoms and so render possible the earlier diagnosis, not only of hæmorrhoids, but of rectal cancer.

The history of the treatment of hæmorrhoids is of great interest and has been the subject of an essay published elsewhere (Parks, 1955). Discussion was for long centred on the choice of the three classical methods of treatment, excision, ligation, or cautery. Excision carried with it the risk of fatal hæmorrhage; ligation was exceedingly painful and was occasionally followed by severe infection; cautery was subject to all three risks. The great practical advance in hæmorrhoidal surgery was made by Salmon (Allingham, 1888) when he showed that the main blood-supply of the anal canal was derived from the superior hæmorrhoidal artery and that the pile covered by sensitive anal epithelium could be severed from its bed leaving a pedicle of superior hæmorrhoidal vessels and rectal mucosa only. Dissecting above the tissues innervated by somatic nerves he was able to ligate the superior hæmorrhoidal vessels without causing pain.

As a result, in Great Britain dissection and ligature has been used to the virtual exclusion of other methods; in America dissection and suture occupies a similar position. Two modifications of Salmon's operation are in vogue at the present time; one described by Miles in 1919, the other by Milligan, Morgan, Jones, and Officer in 1937.

Miles drew down the internal hæmorrhoid with his pile clamps, made a V-shaped incision in the anal skin with the base of the V at the mucocutaneous junction and tied a strangulating ligature around the pedicle. The ligature enclosed a portion of sensitive anal mucosa and a great deal of pain followed his operation, so much so that continuous sedation was necessary for three days afterwards. All his patients had urinary difficulties for 20 hours. As for results, he said: "This method of operating yields 100 per cent of successful results. I have performed 5000 operations in this way with uniform success."

The modification of Milligan and others differs little from that of Miles. They specifically state that the skin incision should cease at the mucocutaneous junction, thereby inevitably leaving an area of sensitive stratified mucous membrane in the pedicle formed. This pedicle is produced by dissecting off the external hæmorrhoidal plexus from the underlying sphincter until a band of fibrous tissue is seen emerging from the muscle. The band, which they called the anal intermuscular septum, is not divided but remains in the pedicle. A transfixion ligature is placed through the band and vascular pedicle and tied. By this means they claimed to anchor the rectal mucosa down to the anal intermuscular septum, preventing mucosal retraction and the formation of a bare area. It is apparent that the transitional zone of stratified epithelium supplied by the inferior hæmorrhoidal nerve is incorporated in the ligature; this can be correlated with the well-known fact that the operation is followed by a considerable amount of pain. Apart from their operative description Milligan and others made new contributions to anal anatomy which will be discussed later.

* Based on the anatomical and surgical parts of a thesis for which the degree of Master of Surgery (Oxon) was granted.

It is interesting to compare the above two methods with Allingham's description of Salmon's operation. Modern authors believe that high ligation results in stricture because of areas denuded of rectal mucosa. Their low ligations are followed by much pain as a rule. Salmon started his incision just below the

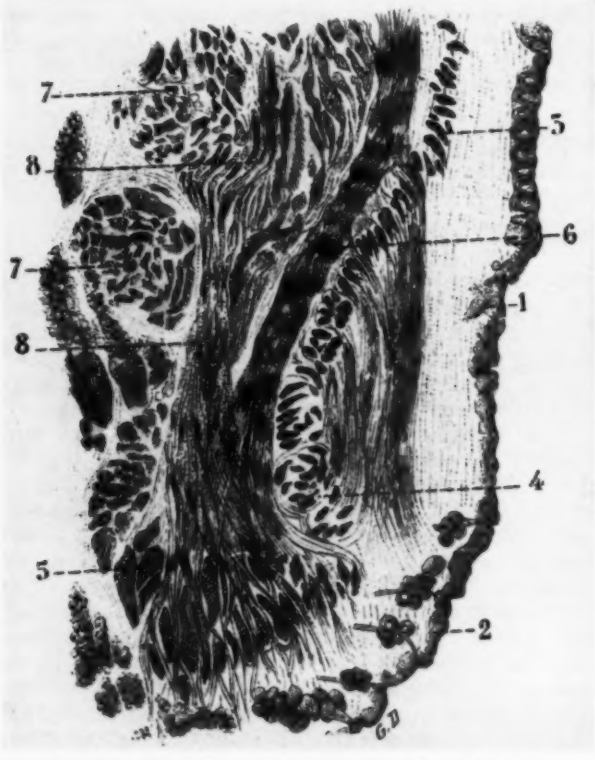

FIG. 374.—A diagrammatic section of the anal wall by Roux (1889): (1) Muco-cutaneous junction; (2) Anal skin; (3) Circular muscle of rectum; (4) Internal sphincter; (5) Subcutaneous external sphincter; (6) Longitudinal muscle; (7) Superficial and deep parts of the external sphincter; (8) Levator ani. (*Reproduced by kind permission of the publishers of 'Traité d'Anatomie Humaine', by J. L. Testut. Paris: Octave Doin.*)

mucocutaneous junction and carried it well into the rectal mucosa. As a result his patients suffered only three to four hours pain.

Few articles on immediate and late results of ligature operations have been published. Anderson (1909) followed up three hundred cases of hæmorrhoidectomy performed at St. Mark's Hospital. Of those subjected to the standard ligature operation then practised, 10 per cent had severe pain requiring more than one injection of morphine; 57 per cent had moderately severe pain and needed one injection; 40 per cent required digital dilatation post-operatively because of a degree of anal stenosis; 5 per cent needed instrumental dilatation. Two patients developed fissure-in-ano. On five occasions severe hæmorrhage occurred; three of these were reactionary, two secondary. The patients were in hospital on an average for twenty-one days. The length of follow-up to detect recurrence was inadequate. Discussing healing Anderson said: "During the third and fourth week the wounds become smoother and more linear, and there may be noticed more or less contraction of the anal canal, the stenosis being most marked where the ligatures have been applied—that is at the upper part of the wound. In six to eight weeks the anal canal feels fairly smooth, but a few subsiding tags may be present at the anal margin."

Gabriel (1920) investigated the incidence of post-operative hæmorrhage at St. Mark's. In a series of 408 ligature operations there were 5 cases of severe secondary hæmorrhage and 2 of reactionary hæmorrhage.

Turell (1952) has described his modification of Earle's operation which may be taken as representative of current American practice. He dissects the pile off the underlying muscle to a point above the pectinate line, clamps the pedicle so formed, excises the pile, and sutures over the clamp. This suture stops short of the pectinate line and so avoids incorporating sensitive anal mucosa in it. The anal wound is left open to allow free drainage. Of 535 cases of his own operation, he was able to follow-up only 249 for a period of about two years. He said: "They failed to show any evidence of recurrence of hæmorrhoids, anal deformity, or stricture necessitating operation."

Turell condemns operations of the type described by Earle (1911) and Mitchell (1903) in which the pile is clamped and completely oversewn. Infection is common in anal wounds which lack free drainage.

ANATOMY

Differences of opinion about anal anatomy have existed between anatomists and clinicians for a long time. An illustration by Roux represents the views of academic anatomists (*Fig.* 374). The internal sphincter is seen to form the muscular wall of the whole of the anal canal. The conjoined termination of the levator ani and the longitudinal muscle of the rectum surrounds the internal sphincter and splits at its lower end into a brush of fibrous tissue strands which intersect the subcutaneous external sphincter and divide it into a number of small fasciculi. These strands terminate by obtaining a firm attachment to the peri-anal skin. The subcutaneous external sphincter is shown to be an aggregation of small muscle bundles, none of which attains any great size.

The epithelial lining of the anal canal was well described by nineteenth century anatomists. Duret (1879) divided it into three zones; cutaneous, middle, and mucosal. The cutaneous zone consists of true skin of the anal verge and the squamous stratified epithelium of the anal canal. The middle zone or 'zone fibroïde' is a stratified layer of mucous secreting epithelium which is found in the region of the anal valves. It represents the position of the embryonic anal diaphragm and its submucosa is well endowed with fibrous tissue. The transition from cutaneous to middle zones is called the muco-cutaneous junction. The mucosal zone consists of true columnar epithelium and continues upwards as the rectal mucosa. The region of transition between skin and columnar epithelium was first called the pecten by Stroud (1896) and was discussed at length by Miles (1944). It varies from 1·5 to 2 cm. in length. Miles ascribed the fibrous tissue contained in the submucosa to chronic inflammation resulting from piles or fissure, but Fine and Lawes (1939) were able to demonstrate it in infants and showed that there

is a considerable amount of smooth muscle present as well.

Milligan and others have contributed two papers on anal anatomy, the first in 1934 being chiefly concerned with the arrangements of the anal musculature in relation to fistulæ; the second, in 1937, dealt more with mucosal anatomy and its application to the surgery of hæmorrhoids. Their views are now widely accepted in this country. They stated that the subcutaneous external sphincter is a discrete muscle mass forming the wall of the lower third of the anal canal (*Fig.* 375). Their views to say that it does not exist. The conflict is centred around the relationship of the internal and external sphincters. If the anatomists are correct an anal intermuscular septum within the anal canal is an *a priori* impossibility for only one muscle forms the wall of the anal canal.

I was stimulated to re-investigate this problem by an observation made while performing the operation of hæmorrhoidectomy shortly to be described. In this procedure saline is injected under the skin and mucosa of the anal canal and freely lifts them off the underlying muscle at all but one point. The

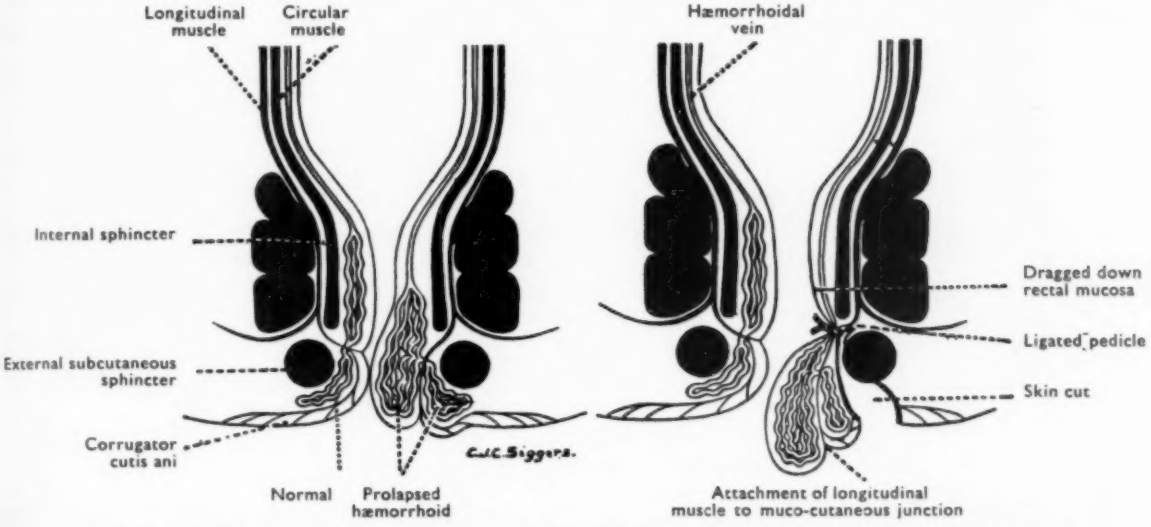

FIG. 375.—A diagram of the anal canal by Milligan, Morgan, Jones, and Officer (1937). *(Reproduced by kind permission of Mr. E. T. C. Milligan and The Lancet.)*

on the termination of the fibres of the longitudinal muscle were at variance with those of anatomists, for they described most of it as forming a fibrous tissue strand passing between the internal sphincter and the subcutaneous external sphincter to be inserted into the mucocutaneous junction. This strand, called the anal intermuscular septum, was said to separate the internal hæmorrhoidal plexus in the submucous space, from the external hæmorrhoidal vessels in the perianal space. The latter is important and their description of it will be quoted.

"It is limited above by the longitudinal muscle at its insertion at the anal intermuscular septum, and by the lateral extension of the longitudinal muscle between the subcutaneous and superficial external sphincters. Superficially the space is bounded by the skin and the m. corrugator cutis ani. Externally the space becomes continuous with the ischio-rectal fossa, but its outer limit may be taken to correspond with the outer edge of the subcutaneous external sphincter. Contained in the space are the external hæmorrhoidal plexus and the subcutaneous external sphincter."

In the living subject the septum was said to cause a well-marked groove between the two hæmorrhoidal areas which is readily visible at operation when traction has been made on the perianal skin.

From this brief review it is apparent that there is no unanimity of opinion on the subject of anal anatomy. Anatomists have never described the intermuscular septum; Wilde (1948) goes so far as interhæmorrhoidal groove described by Milligan and others is greatly exaggerated by this manœuvre which clearly demonstrates that there is only one line of attachment of the mucosa of the anal canal. This is the line of the anal crypts. During the operation the external hæmorrhoidal plexus is dissected off the underlying muscle; at a certain point a strand of fibrous tissue is met which connects the muscle and the anal mucosa at the line of the crypts. It corresponds with the description given by Milligan and others of the anal intermuscular septum. When it is cut it is seen to have been attached to the fascial layer on the internal sphincter; there is no muscular gap to suggest a junction between two separate muscles. According to Milligan and others the muscle which first presents at the anal margin is the subcutaneous external sphincter. Eisenhammer (1951, 1953), however, has shown that the internal sphincter reaches the anal verge and he thus supports the views of the nineteenth-century anatomists. I have also found by biopsy that the muscle ring, which lies under the anal margin, is usually the lowest fasciculus of the internal sphincter. On palpation a depression is felt between the adjacent internal and subcutaneous external sphincters as Milligan and others described, but it does not lie immediately beneath the mucocutaneous junction as they suggested. They confused a visible depression (the line of the anal crypts) with a palpable groove occurring lower in the anal canal.

In order to obtain a more detailed knowledge of the anatomy of the anal canal, specimens obtained at post-mortem examination and following abdomino-perineal resection of the rectum have been examined. later. It is only necessary now to state that th were examined histologically after the submuco and marginal spaces had been infiltrated with fluid order to reveal the anatomy more distinctly.

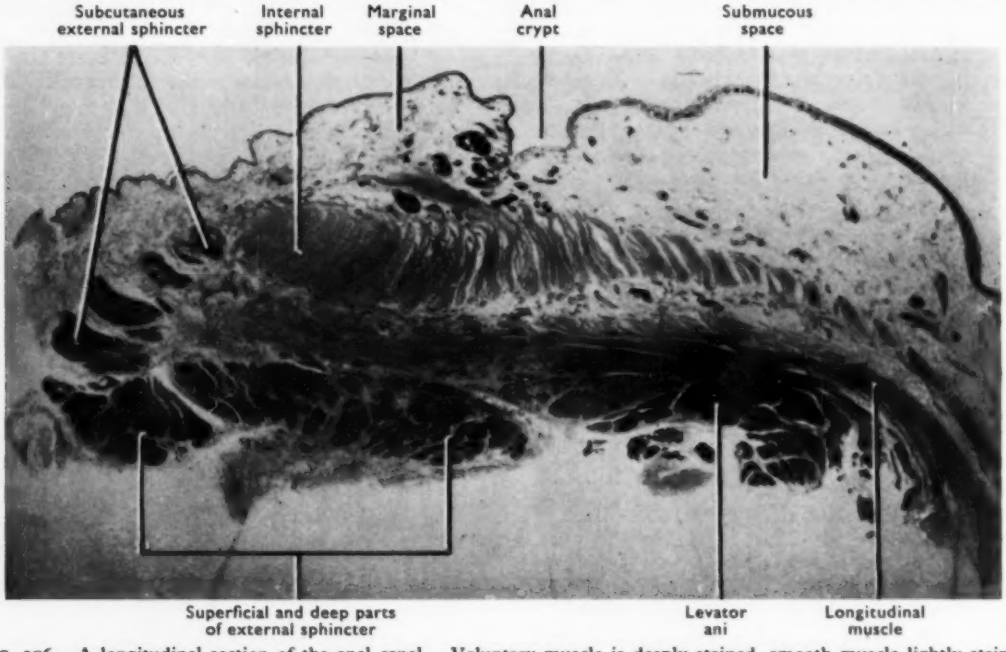

FIG. 376.—A longitudinal section of the anal canal. Voluntary muscle is deeply stained, smooth muscle lightly stained. Note smooth muscle fibres streaming off the internal sphincter to help form the mucosal ligament.

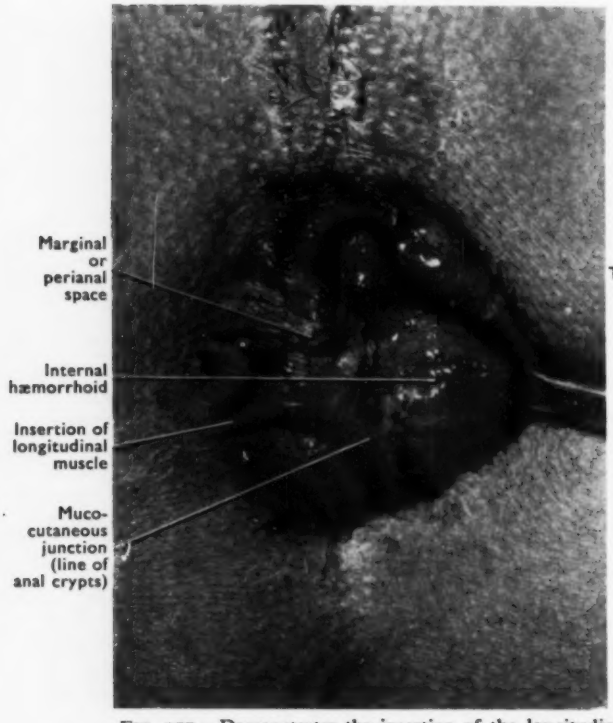
Marginal or perianal space
Internal hæmorrhoid
Insertion of longitudinal muscle
Muco-cutaneous junction (line of anal crypts)

FIG. 377.—Demonstrates the insertion of the longitudinal muscle lateral to the marginal space and shows the inter-hæmorrhoidal depression caused by the attachment of the mucosal ligament.

FIG. 378.—After dissection of the external hæmorrhoidal plexus, the insertion of the most medial strand of the longitudinal muscle is seen. The lowest part of the internal sphincter and a small bundle of the subcutaneous external sphincter are also visible.

A preliminary communication on this investigation has been published (Parks, 1954); a detailed account of the preparation of the specimens will be published

In general the views of anatomists are confirmed The internal sphincter is found to form the wall the whole anal canal though occasionally a sma

bundle of the subcutaneous external sphincter may occupy the terminal position (*Fig.* 376). The latter muscle is split into bundles by the terminating fibres of the conjoined levator ani and longitudinal muscles. The longitudinal muscle is attached to the anal skin over a considerable area but the greater part is concentrated at the anal margin and forms a distinct ring around the anus (*Fig.* 377). This insertion separates the marginal or perianal space from the ischiorectal fossa. No one fibrous band was found which would justify separate description as an intermuscular septum.

The anatomy of the epithelium and the subepithelial space justifies detailed description because it was found to differ considerably from current description. At the anal margin there is a gradual transition from true skin, with sweat-glands and hair follicles, to stratified squamous epithelium. This junction, which I have called the squamous border, overlies the area of apposition of the lowest fibres of the internal sphincter with the most medial bundle of the subcutaneous sphincter. Through the gap between the two muscles passes the most medial of the terminating strands of the longitudinal muscle which gains a firm attachment to the skin of the anal verge (*Figs.* 378, 379). Stratified squamous epithelium continues for 1–1·5 cm. within the anal canal, changing to a layer of stratified columnar epithelium at the level of the anal crypts. Though a sharp distinction has been made between skin and stratified squamous epithelium this is not wholly justified as an occasional sweat-gland or hair follicle is found in the zone.

The zone of stratified columnar epithelium (the middle zone) usually commences in the depths of the anal crypts and extends upwards from 0·25 to 1 cm. in length. The surface is mucus-secreting and moist in contrast to the zone below the crypts which is keratinized and dry. The nerve-supply appears to be subject to variation, but I have found during the performance of many routine proctoscopic examinations that this epithelium is, as a rule, highly sensitive (cf. Milligan and others, 1937).

The change from stratified epithelium to rectal mucosa occurs 0·25–1 cm. above the crypts; macroscopically it is seen as a wavy line and is called the pectinate or dentate line. The internal hæmorrhoidal plexus, commencing just above the crypts, is covered by glandular rectal epithelium with the exception of the lowest point, which is covered by the stratified columnar zone. Chronic prolapse stimulates the stratified layer to spread upwards over a pile, thereby encroaching on the territory of glandular epithelium. Ewing (1954) made a careful study to clarify the exact situation of Hilton's line. He found Hilton's description of anal anatomy to be incomplete in many respects and was unable to identify the white line, either from Hilton's original essay or from clinical observation. He therefore advocated that the term " the white line of Hilton " be abandoned, and my own investigation entirely supports his view.

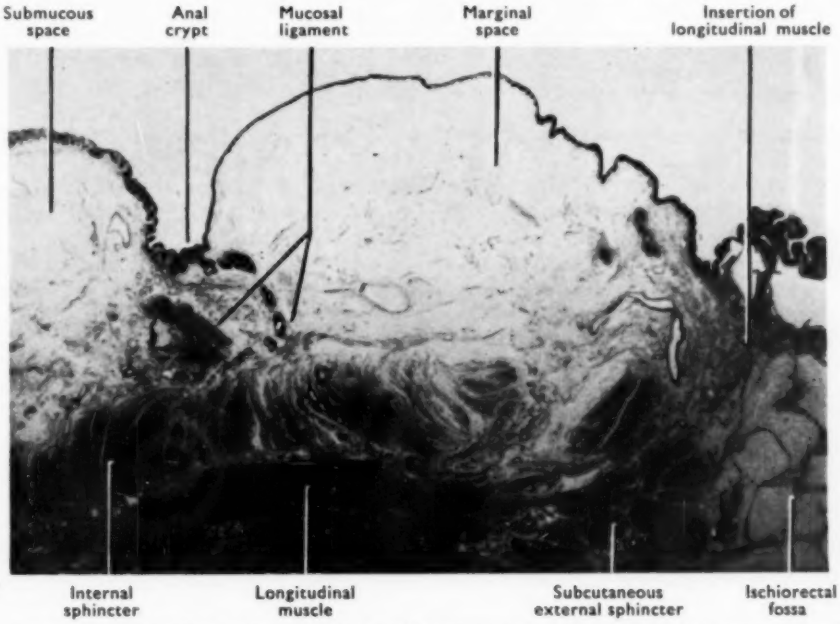

FIG. 379.—A longitudinal section of the anal canal which demonstrates the relationship between the submucous space, the marginal space, and the ischiorectal fossa. Note anal gland penetrating internal sphincter.

The anatomy of the subepithelial space has been found to differ from the description of anatomists, who give only a meagre account, and also from that of the clinicians. The injection of saline into the space has revealed structures which have not hitherto been observed in the preserved specimen. In life the space is distended with the blood in the hæmorrhoidal veins which lifts the mucosa off the muscle and shows up any underlying attachment which may exist. In preserved tissues the mucosa lies flat on the muscle and the characteristic anatomy of the submucosa is concealed. By an injection technique I have been able to show that the fibromuscular tissue of the submucosa is not haphazard in its arrangement but follows a definite pattern. The groove between the two hæmorrhoidal plexuses as

described by Milligan and others is clearly seen. It occurs approximately at the midpoint of the anal canal and is caused by the adherence of a fibromuscular band to the mucosa which I have called the mucosal suspensory ligament (*Figs.* 376, 379). The constitution of this is complex. It has three components: the muscularis mucosæ, muscle-fibres from the internal sphincter, and fibrous tissue from the fascia surrounding the fasciculi of the internal sphincter. Numerous fibrous strands intersect the internal sphincter; they join on the internal surface of the muscle to form a fascial layer of canal is not generally recognized. It can be inverted or everted with ease, hence the difficulty which arises when the operator is trying to identify a structure at a given level in the canal.

The conclusions I have formed are shown diagrammatically in *Fig.* 380. Previous authors have described the fibromuscular tissue of the anal submucosa; Fine and Lawes (1939) suggested that there was a tethering of the mucosa at the line of the anal valves, but as far as I am aware the mucosal ligament has not been previously described. It has considerable significance in relation to anal disease. In the

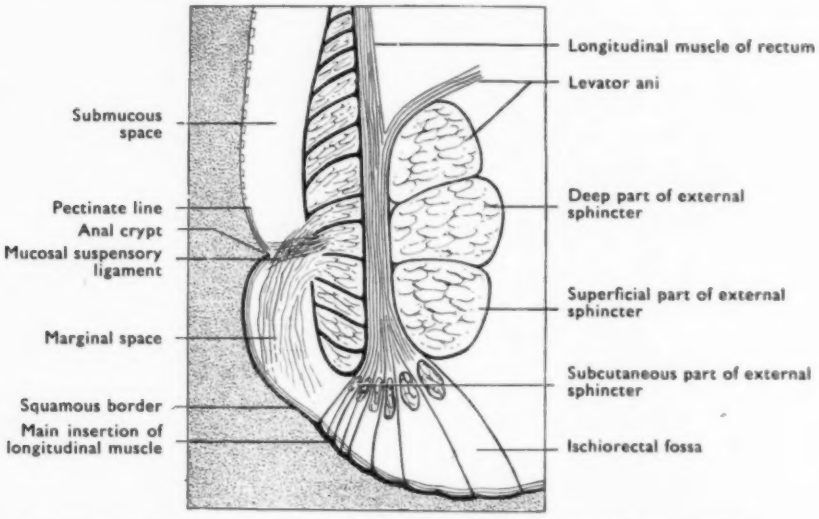

FIG. 380.—A diagram to summarize the anatomical findings described in this article.

maximal thickness at the midpoint of the anal canal. From this point the mucosal ligament passes out to gain a firm attachment to the mucosa of the anal crypts and to a less extent the tissue between them. By this arrangement a ring of fibrous tissue and smooth muscle is formed around the anal canal firmly anchoring the mucosa to the muscle wall.

It will be seen that the mucosal ligament divides the subepithelial space into two compartments; superiorly is the submucous space containing the internal hæmorrhoidal plexus; below is the space containing the external hæmorrhoidal veins and named the perianal space by Milligan and others. It is limited inferiorly by the main insertion of the longitudinal muscle into the skin of the anal verge. As the greater part of this space lies within the anal canal it is hardly appropriate to call it perianal; I prefer to call it the marginal space. It is richly endowed with fibrous tissue and is not readily distensible; this no doubt accounts for the intense pain engendered by a perianal hæmatoma. Partial prolapse, or traction on the perianal skin during the operation of hæmorrhoidectomy, produces eversion of the anal canal and causes the space to lie outside the canal. Migration of the space over the anal verge also occurs when it is distended in the presence of third degree prolapsing hæmorrhoids or by a thrombosis in the external hæmorrhoidal plexus. When the cause of distension subsides the stretched skin forms a perianal tag. The mobility of the anal normal individual it prevents mucosal prolapse. At all other points the mucosa will glide smoothly on the underlying submucosa and will give way in front of a hard scybalous mass of fæces; at this point, however, it is fixed and may be torn during the passage of a constipated stool, particularly if sphincteric spasm is present. It tends to limit the spread of blood or pus between the submucous and marginal spaces. It will be noted that the marginal or perianal space is completely walled in by the mucosal ligament, the internal sphincter, and the terminating longitudinal muscle. This is reflected clinically by the fact that thrombosis in the external hæmorrhoidal plexus, and perianal abscesses, are strictly limited in extent; they do not spread into the ischiorectal fossa.

The macroscopical anatomy of the anal epithelium is the result of the arrangement of the submucosal fibrous tissue. We have seen that the crypts are formed in part by the attachments of the bands of the mucosal ligament; similar though more attenuated strands extend upwards from the line of the crypts and are attached to the mucosa between the anal columns causing the intercolumnar depressions. The columns themselves are redundant folds of mucosa allowing the functional dilatation of the anal canal.

Observations I have made at operation when using the expanding retractor necessitate a slight change in the usual description of internal hæmorrhoids. Most authors depict them as pear-shaped

swellings protruding into the anal canal from a well-defined pedicle. If the anal canal were incised and laid open this state of affairs would be represented by *Fig.* 381. When the expanding speculum is used the hæmorrhoid is seen to have a triangular shape with its base in the rectum and its apex at the line of the anal crypts as illustrated in *Fig.* 382.

When hæmorrhoids are present a diffuse change commences in the rectal epithelium from three to five centimetres above the mucocutaneous junction. It is seen as a slight elevation of the mucosa together with a deepening in hue. The change becomes more marked as the mucocutaneous junction is approached and is concentrated into three major piles. With the increasing severity of the condition the hæmorrhoids become less discrete and the entire mucosa is changed into a mass of primary and secondary piles.

The anal canal is well endowed with blood-supply. The superior hæmorrhoidal plexus is served by the arterial arrangement described by Miles (1919). The marginal space is supplied by branches of the inferior hæmorrhoidal artery. Anastomosis across internal and external sphincters is abundant. Duret showed that the line of the anal crypts forms a watershed of venous drainage between superior and inferior hæmorrhoidal veins. Extensive communication exists across the sphincters. In patients

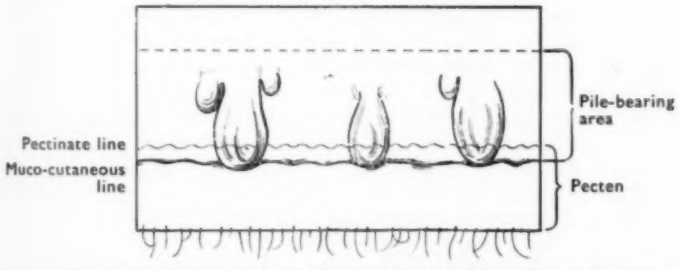

FIG. 381.—The current concept of hæmorrhoids. The anal canal has been laid open.

with third degree piles the superior and inferior hæmorrhoidal plexuses become joined together so that the watershed no longer exists. So great is the arterial supply of some hæmorrhoids that writers have been led to assert an angiomatous or inflammatory basis for them. It is more probable that the cause of this excessive vascularity is the presence of arteriovenous shunts in the submucosa of the anal canal. This would account for the clinical observation that pricking this variety of pile during injection treatment often results in a pulsating stream of oxygenated blood.

AETIOLOGY

Many explanations have been put forward to account for the occurrence of piles. Ancient and medieval writers adhered to Hippocratic dogma; Stahl (1729) considered piles to be nature's safety valve in plethora of the portal system; Copeland (1870) indicted spasm of the anal sphincters; Pennington (1923) and several American authors believed infection and thrombosis of the internal hæmorrhoidal plexus to be aetiological agents. Most writers mention heredity as playing a part but this is difficult to prove in a condition said to be present in seventy per cent of people over the age of forty years (Miles, 1944). Morgagni (1749) was the first to enunciate a scientific account of the cause of hæmorrhoids and his views are still widely held to-day. He believed that the erect posture results in such an increase of pressure in the lower tributaries

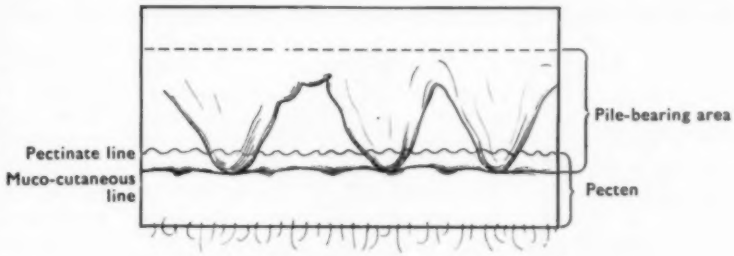

FIG. 382.—The author's concept of hæmorrhoids.

of the portal vein that these veins dilate to form hæmorrhoids (*see* Parks, 1955).

Difficulties arise in all these hypotheses. Morgagni himself was not satisfied with his own explanation because, as he pointed out, it did not account for the occurrence of varicosities in the anal canal alone. This stumbling block is present in all hypotheses which cite a general rise in portal pressure as an aetiological factor. It applies equally to Verneuil's view (1855) that the veins are occluded as they pass through the rectal musculature some ten centimetres above the anus. Satisfactory reasons must be found to account for the fact that hæmorrhoids are localized to the upper half of the anal canal; that constipation is universally accepted as a contributing agent; and that the presence of pelvic tumours, especially a pregnant uterus, exaggerates the condition.

In 1879 Duret gave one of the best accounts which have been written on this subject. He subscribed in part to Morgagni's hypothesis but, in addition, he believed that transient increase in portal pressure due to straining, particularly at stool, was a contributing factor of great importance. We know that intrarectal pressure may rise from a normal of 20 mm. of mercury to 200 mm. during these efforts (Best and Taylor, 1939). If pressure in the superior hæmorrhoidal veins were readily transmitted to the external hæmorrhoidal vessels the force available to distend the internal hæmorrhoids would be rapidly dissipated. Duret, however, showed that there is very little anastomosis between the two groups of veins in the submucous layer, though there are numerous communicating channels penetrating the sphincters. During an effort of abdominal straining the anal sphincters contract and cut off the sphincteric anastomoses. He believed that this resulted in the internal hæmorrhoidal plexus receiving the maximal effect of portal hypertension, but the argument still does not satisfactorily account for the fact that piles are confined to the anal canal. Few patients with cirrhosis of the liver complain of piles; in a recent

article on portal hypertension Taylor (1954) said, "we have yet to see a portal hypertensive patient present himself with a chief complaint of hæmorrhoids". The same author measured the pressure normally found in the superior hæmorrhoidal vein; he found it to be 25 centimetres of water when the patient was supine and 45 centimetres when erect.

The cause of hæmorrhoids must be sought in the anatomy and function of the anal canal. In the normal individual with a competent anal sphincter the rectal ampulla is not in contact with atmospheric

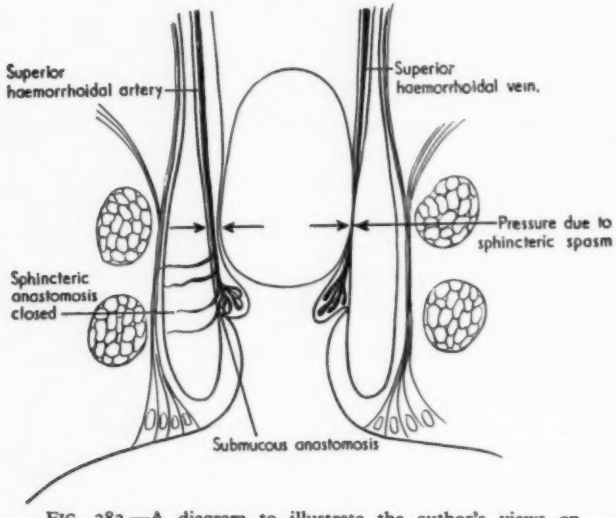

FIG. 383.—A diagram to illustrate the author's views on aetiology.

pressure; its pressure is the same as that of the rest of the pelvis. During defæcation the rectal mucosa undergoes a minor degree of reversible prolapse and comes into contact with the atmospheric pressure. If portal pressure is to exert any effect on the anal veins it can only be at this time, for they are then unsupported and may easily dilate. Only by this modification can Duret's views be held to give a satisfactory explanation for the formation of piles.

None of these hypotheses, however, is entirely convincing; they all fail to account for the characteristic location of the primary hæmorrhoids on the anal circumference. I would therefore like to advance a postulate which I believe to fit the fact more satisfactorily.

During the efforts to expel a constipated stool the fæcal mass is impacted in the lower part of the rectal ampulla and exerts considerable pressure on the rectal wall (*Fig.* 383). Between the scybala and the muscle wall lie the mucosa and submucosa containing the superior hæmorrhoidal vessels. Pressure in the veins is not very high and the venous return is readily cut off; the greater arterial pressure, however, will enable blood to reach the superior hæmorrhoidal plexus. Duret maintained that there is little connexion between the internal and external hæmorrhoidal veins in the submucous layer and that the sphincteric anastomosis is cut off by muscle action. If this be true, the situation is established in which arterial blood reaches the superior hæmorrhoidal plexus but is unable to escape from it until the venous pressure rises to a considerable height. This will lead to dilatation of the superior hæmorrhoidal plexus, especially in the neighbourhood of the termination of the superior hæmorrhoidal arteries. In this way we can satisfactorily explain the situation of the three primary hæmorrhoids. The high pressure developed in the veins during the passage of a constipated stool explains the bleeding which is so characteristic of first degree piles. Blood appears during or just after the passage of a motion, often as a jet indicating the high pressure at its source. Its bright red colour is evidence that it has not long left its artery of origin.

Once a dilated venous plexus has been established, partial prolapse will occur with each bowel movement. This will first take place as an overriding of the internal hæmorrhoid over the mucosal ligament. For a while the pile returns to the canal after each bowel movement (second degree hæmorrhoid), but with the increasing duration of prolapse the mucosal ligament becomes stretched and disappears altogether. The anal mucosa is now free to prolapse with any increase in intra-abdominal pressure and will not return spontaneously. A third degree pile is thus a sliding hernia of the anal mucosa. Furthermore the disappearance of the mucosal ligament allows free communication to take place between the submucous and marginal spaces. The superior and inferior hæmorrhoidal veins are then free to anastomose; the marginal veins dilate and an intero-external pile is formed. When at this stage the passage of a hard fæcal mass occludes the superior hæmorrhoidal veins, blood can flow readily into the external plexus and there is no great rise in pressure in the internal pile. As a result the pile is not so tense, is not so easily damaged by a hard stool, and therefore bleeds less readily. Other factors responsible for the diminished tendency to bleed are chronic prolapse which causes squamous metaplasia of the rectal mucosa and recurrent minor thrombosis which increases the amount of fibrous tissue in the pile.

TREATMENT

Proper treatment of hæmorrhoids can only be founded upon sound aetiological concepts. If the mucosal ligament has not been stretched it is reasonable to thrombose the pile by injection and to encourage the patient to establish satisfactory bowel habits. Once the ligament has been stretched the condition is irreversible and only operation offers hope of cure. A satisfactory surgical cure depends not only upon removal of dilated veins; more important is a high ligation of the superior hæmorrhoidal arteries and the production of submucous fibrous tissue to prevent prolapse and venous distension of the submucous space. Ball (1908) was surprised at the dramatic effect of apparently inadequate operations on cases of advanced piles; he believed this to be due to the mucosal fixation produced. I believe that Whitehead (1882) was in error in thinking that he could eradicate piles by excision of the pile-bearing area. If primary union occurs after his operation a new pile-bearing area is formed upon which the causative factors continue to work. A great deal can be done to prevent recurrence after any operation by encouraging the patient to establish normal bowel habits. He should be taught to relax the anal sphincters during defæcation and to

avoid continual straining. Prolonged and ineffectual attempts to obtain a bowel motion should be discouraged; novel reading and meditation are forbidden.

Submucous Hæmorrhoidectomy. — The purpose of an operation for hæmorrhoids must be a successful cure with as little discomfort and disability as possible. From the foregoing considerations it will be seen that cure depends on three factors; the removal of most of the dilated veins; high ligation of the hæmorrhoidal arteries; and fixation of the anal mucosa to the underlying muscle to prevent prolapse and to obliterate the submucous space.

Most operations for hæmorrhoids are notorious for the amount of discomfort they cause. We have seen that much of the pain in the post-operative period is due to the incorporation of sensitive anal mucosa in the ligature and to the presence of the tube and packs. Ligation of the hæmorrhoidal arteries above the muco-cutaneous junction will therefore not only be more curative but less painful than the low ligature described by Miles and by Milligan, and others. A possible disadvantage is that bleeding points may occur above the anorectal ring which are not compressed by contraction of the sphincters.

Another factor causing post-operative pain is the presence of large areas of anal wall denuded of epithelium. These areas may cause anal spasm, painful bowel actions, and the late occurrence of fissure-in-ano. Constant spasm narrows the anal canal and if fibrous tissue is deposited it will cause stenosis. If an operation can be restricted to the removal of primary piles alone it is not difficult to avoid the creation of large bare areas, but when secondary piles are present it is often impossible to excise them without running a serious risk of stricture. There are no recent statistics on this subject but in Anderson's series (1909) at St. Mark's Hospital 40 per cent of the patients required digital dilatation following ligature operations and 5 per cent needed instrumentation. To avoid spasm, stricture, and fissure early healing of the wounds is essential.

Jean Louis Petit (1774) one of the founders of modern surgery, observed that the epithelial covering of the pile was the sensitive part and that if it were first incised the hæmorrhoidal plexus could be ligated with less post-operative pain. He therefore modified the ligature operation by dissecting off the skin and mucosa before transfixing the vascular tissue beneath. He claimed that by this means healing was more rapid and that the two mucosal flaps covered the hæmorrhoidal pedicle to act as hæmostatic agents. Samuel Cooper (1809) practised the same technique and considered that it was not so prone to be followed by stricture as were other operations (*see* Parks, 1955).

As many problems of hæmorrhoidal surgery were solved by this technique it is perhaps surprising that it did not become universally accepted. One objection is apparent; it must have taken longer to perform than ligature or excision, a matter of great importance before the days of general anæsthesia. There is no doubt that it was more difficult (Copeland, 1810).

For these reasons the method was not generally adopted and gradually lost adherents. The success and simplicity of Salmon's operation resulted in the abandonement of Petit's technique. In 1941 Calman re-introduced the principle. For second degree piles he made a ⊥ shaped incision in the anal mucosa. The vascular plexus was dissected from underneath the mucosa, ligated, and excised. For third degree piles the incision was carried out into the anal skin. The results were most encouraging; his patients experienced little post-operative pain and had no undesirable sequelæ of any kind. However, even in America, the operation was not adopted and no reference has been made to it in the post-war literature. The reasons were probably the same as those which led to the rejection of Petit's attempt to establish the technique. The dissection of mucosal flaps is difficult, tedious and is accompanied by much bleeding if vascular hæmorrhoids are present.

Theoretically, however, the principle has everything to commend it. Early healing is assured because bare areas are immediately covered by mucosal flaps. In the next section I shall describe a technique I have adopted to overcome the objections to the method. The operation is performed under direct vision by using a self-retaining speculum. Saline infiltration is used to open up tissue planes making it possible to dissect between the mucosa and the vessels of the submucosa. I have now performed this operation on more than one hundred occasions and in the section which follows the result of the first fifty cases will be reported.

THE OPERATION

The patient is admitted to hospital two days before operation. Liquid paraffin, 1 oz. twice daily, is administered throughout the period of hospital treatment unless diarrhœa occurs. The night before operation an enema is given, followed by a colon wash-out the next morning; a clean rectum minimizes the risk of infection of the hæmorrhoidal bed. Sulphonamides have not been used. General anæsthesia is administered, combined with muscle relaxant drugs to facilitate the introduction of the rectal speculum. Local analgesic infiltration is adequate, however, should the need arise. The lithotomy position gives the best exposure of the part; skin preparation and towelling are as for any other anal operation.

Operative Technique.—The piles are inspected by applying hæmostatic forceps to the peri-anal skin; it is necessary at this stage to decide the extent of the dissection required and whether or not there are secondary hæmorrhoids to be dealt with. The speculum illustrated in *Figs.* 384, 385 is then inserted into the anal canal to expose the right posterior pile. The instrument is designed so that the anal sphincters shall grip it in the groove near the handle; the expanded blades dilate the rectal ampulla. The speculum is of great help, not only for hæmorrhoidal surgery, but also for operating upon fissure, fistula, and benign ampullary neoplasms. After insertion the blades are separated and cause moderate stretching of the anal sphincters. Normally the three standard incisions are made, left lateral and right anterior and posterior, small secondary piles being removed by extending the submucous dissection to include them; but if a

large secondary pile is present, as often occurs in the posterior position, it is removed through a separate incision.

The keratinized zone of anal epithelium is picked up with a hæmostat just below the muco-cutaneous line (*Fig.* 386). The sulcus between the internal and external hæmorrhoidal areas is readily seen; it is at this point that the mucosa is adherent to the muscle by the fibrous band which I have already described. Submucous infiltration with saline containing one part of adrenaline per 400,000 is com-

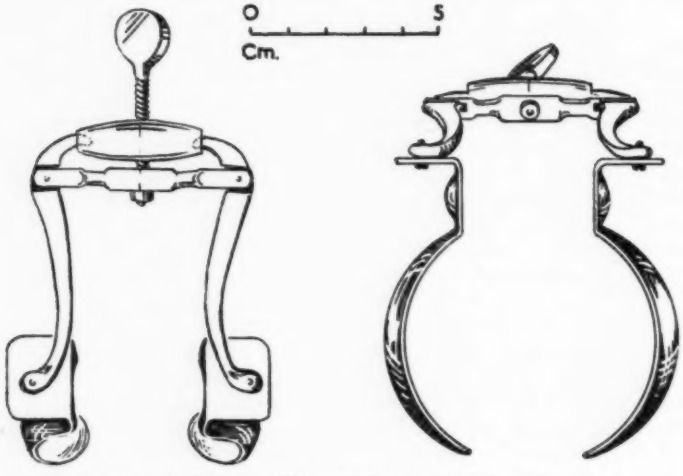

FIG. 384.—A diagram of the author's retractors, drawn to scale.

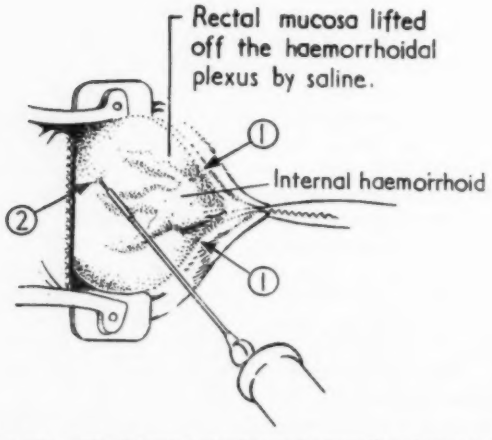

FIG. 386.—The injection of saline and adrenaline, first at 1, the inter-hæmorrhoidal sulcus, then at 2.

menced in the sulcus as shown. It is necessary to start the injection here because the adherent mucosa is difficult to raise from the underlying muscle unless continued prolapse has resulted in attenuation of the mucosal ligament. This performed, the needle is inserted under the rectal mucosa and the fluid spreads rapidly in all directions. Occasionally the effect of previous sclerosing injections may cause difficulty but this is unusual. Finally the region of the external hæmorrhoidal plexus is infiltrated. Altogether from 30–40 ml. of fluid is injected into each pile mass.

With scissors an incision is made into the surrounding epithelium on either side of the holding forceps. As little as possible of the epithelium of the anal canal is removed. If the keratinized zone of squamous epithelium has been distended by chronic prolapse it will be necessary to excise an ellipse to avoid skin tags. The most lateral part of the incision should reach but not encroach upon the main

FIG. 385.—The self-retaining anal retractor. (*Kindly made to the author's specification by Messrs. Down Bros. and Mayer and Phelps, Ltd.*)

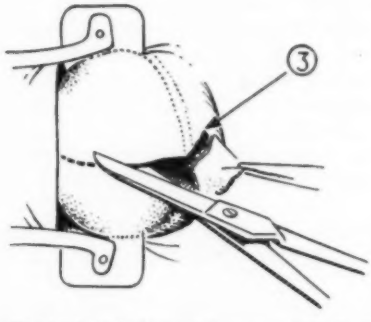

FIG. 387.—The incision into rectal mucosa. The final injection of saline has been placed at 3.

insertion of the longitudinal muscle. An extensive back cut is quite unnecessary and delays healing by many weeks.

This incision is carried forwards around the hæmostat to meet on the rectal side in front of the point of the instrument. Using curved dissecting scissors the anal mucosa in the region of the muco-cutaneous line is undermined for a short distance and in so doing some of the fibres of the mucosal ligaments are severed. A vertical incision is then made into the rectal mucosa from the point of the hæmostat (*Fig.* 387) upwards for about 1 in. The cut edges of the rectal mucosa are undermined with scissors, dissecting on each side to expose the secondary piles. It is essential that the dissection should be carried out in the submucosal layer, for at a slightly greater depth large varices are encountered which bleed profusely and obscure the field of

operation. In this manner two mucosal flaps are formed as shown in *Fig.* 388.

Attention is now directed to the external plexus which is similarly exposed. A plane of separation is found between the internal sphincter and the fibro-muscular tissue forming a sheath on its internal

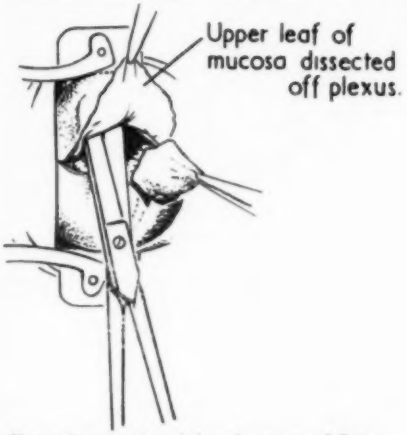

FIG. 388.—Undermining the mucosal flaps.

surface (*Fig.* 389). Traction exerted on the pile deforms the internal sphincter and its fascial covering so that the operator's scissors tend to enter the internal sphincter and remove segments of it (*Fig.* 390). This should be avoided as it opens up fresh tissue planes to infection. Once the fibro-muscular

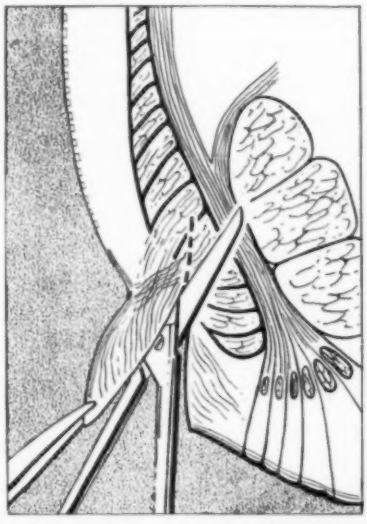

FIG. 390.—A diagram to show the ease with which segments of the internal sphincter may be removed during the detachment of the mucosal ligament from the muscle.

tissue constituting the mucosal ligament has been carefully dissected off the internal sphincter, a plane opens up between the superior hæmorrhoidal plexus and the sphincter muscle (*Fig.* 391). This plane is pursued for an inch above the mucocutaneous junction. The index finger of the left hand is introduced into the space so formed and the hæmorrhoidal plexus drawn down from the anal canal. This manœuvre brings the mucosal flaps into better view enabling the operator to extend them further by sponge dissection. Care must be taken not to lacerate the friable mucous membrane.

When dissection has been completed on both surfaces of the vascular plexus the resulting submucosal tissue containing the hæmorrhoidal vessels has the shape of a wedge with its apex at the tip of the hæmostat and its base in the rectum. The base may be as much as 1½ in. wide and is too great a mass for

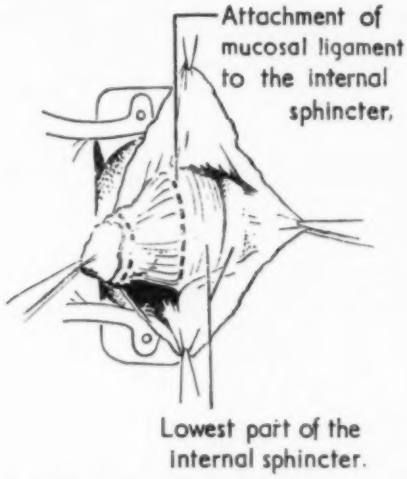

FIG. 389.—Dissecting the hæmorrhoidal plexuses away from the internal sphincter.

one ligature. It may be ligated in parts but it is usually sufficient to cut through the lateral arms of the wedge, leaving a central component which can be readily transfixed. Should the cut sections bleed they must be seized and tied, for they are above the anorectal ring and are not compressed by the anal

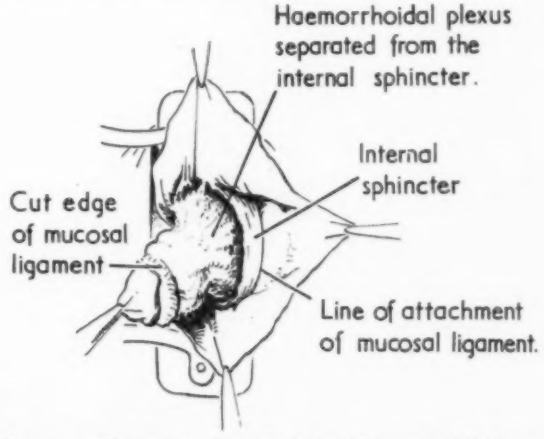

FIG. 391.—The plane between the internal hæmorrhoidal plexus and the internal sphincter has been entered.

sphincters. The pedicle which remains is transfixed with 0 chromic catgut and the excess of hæmorrhoidal tissue is excised (*Figs.* 392, 393). Further search is made for high bleeding arteries. Bleeding from small arteries piercing the sphincters and venous oozing from the cut lateral margins is of no consequence; it stops as soon as the muscle tone returns. Bleeding from the cutaneous verge must be stopped meticulously. When the retractor is closed the mucosal edges are seen to come together and to cover the bare area completely; the ligature is covered by a hood of mucosa. In the case of first

and second degree piles, where the mucosal ligament is intact, no suture of the flaps is necessary; the two edges are automatically opposed and anything which may interfere with the drainage of blood and serum is to be discouraged (*Fig.* 394). With third degree piles, when the mucosal ligament has disappeared as the result of chronic prolapse, it is necessary to fix the flaps to the muscle at the point where the mucosal ligament is to be found normally, with one stitch of

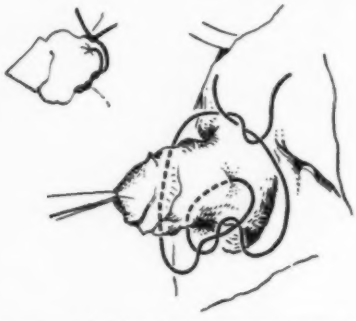

FIG. 392.—Ligating the hæmorrhoidal pedicle.

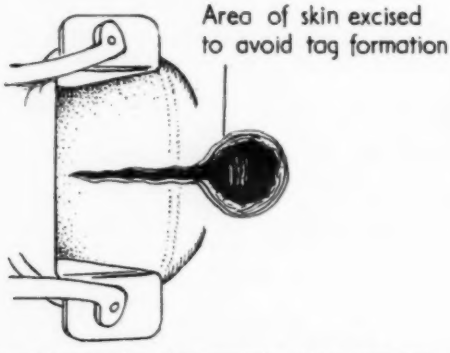

FIG. 394.—The wound at the completion of the operation. Some of the keratinized zone of the anal epithelium has been removed to prevent the formation of skin tags.

00 plain catgut. Failure to do this may result in rectal mucosa slipping down and being grafted on to the cutaneous wound where it may weep and become a source of discharge and irritation.

The left lateral and right anterior piles are then removed in that order. The right anterior pile is the most difficult to see; by angulating the retractor it is possible to illuminate the upper wall of the anal canal. At the end of the operation each pile bed is inspected afresh for bleeding. If the dissection has been performed in the correct plane there is seldom much loss of blood. Œdema during the first few days after operation brings the edges of the wounds together and they heal rapidly. Large secondary hæmorrhoids are now removed through separate incisions in the rectal mucosa only. A secondary pile can be readily excised through a longitudinal incision above the anal crypt line without interfering with the pecten at all. The latter region, rich in submucosal fibrous tissue, is the most common site for abnormal fibrous tissue to occur after operation. It is wise to injure it as little as possible. No dressing or tubes are placed in the anal canal; a pad is put over the natal cleft and maintained in position by a T-bandage.

Post-operative Care.—Post-operative pain is reduced to a minimum by this operation. Soreness rather than pain is experienced and this symptom is usually relieved by codeine and aspirin. Severe pain is unusual and has been experienced only by a few highly-strung subjects. Patients are allowed out of bed within a few hours after operation; this is a

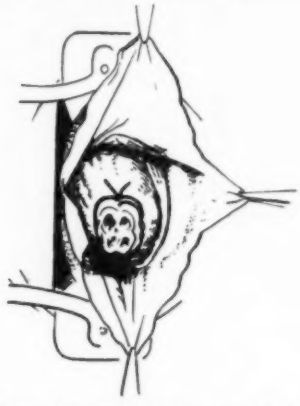

FIG. 393.—Excess hæmorrhoidal tissue has been removed.

great help in overcoming difficulty in micturition. I believe that the administration of morphine is a factor in the production of post-operative retention of urine. The patient's sensitivities are dulled and he does not experience the symptoms of a full bladder. As a result over-distension occurs and he is not able to void. Retention of urine has been rare following this operation.

Liquid paraffin is given to prevent the formation of hard scybala. The first bowel movement takes place spontaneously on the second or third day; enemas are rarely necessary. Pain with the first bowel movement is variable, depending on whether the stool is hard or soft; a soft stool may cause no pain at all. Diarrhœa due to excessive administration of paraffin is undesirable as it prevents the dilatation of the anal canal by the passage of a formed stool. The early establishment of normal bowel habits is of the greatest help in preventing anal stenosis. It is far better that the patient should dilate his anal canal by normal bowel function than by digital or instrumental stretching. He can only do this if there is little pain and no spasm.

There are no large wounds to dress or irrigate and the nursing staff is consequently relieved of much time-consuming treatment. After 48 hours the patient has a daily bath. Rectal examination on the fifth or sixth day reveals a remarkable absence of spasm and causes little pain. The incisions are felt as ridges caused by the œdema of the opposed mucosal edges. The patient is discharged from hospital at the end of a week, by which time he is usually free from pain.

Each week, for three weeks, a rectal examination is performed to ensure that any deposition of fibrous tissue is immediately combatted by digital dilatation. No routine digital or instrumental dilatation is required. At the end of a month proctoscopy is performed to detect the presence of any secondary hæmorrhoids which may have been left behind; if any are found they are treated by injection.

RESULTS OF OPERATION

A series of fifty patients is inadequate, perhaps for the purpose of making final judgement about a new operation, but I believe that the present investigation gives some reliable information about the value of submucous hæmorrhoidectomy. The patients were unselected and treatment was given at two general hospitals. Men exceeded women in the ratio 2·5 to 1. Prolapse was the indication for operation in 85 per cent of cases; previous injection treatment had been received in 20 per cent. The average age of the patients was 43 years.

Prolonged study of these patients is difficult because they are often unwilling to return to out-patient clinics after they have been cured of a condition which does not appear to be serious.

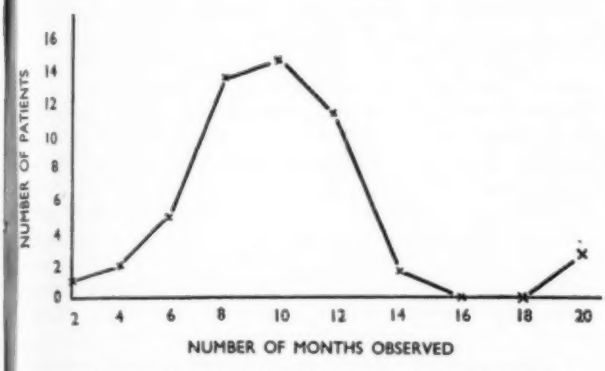

FIG. 395.—A graph to show the extent of the post-operative observation of the patients in this series. The patients are grouped in two-monthly periods.

Fig. 395 illustrates the extent to which these patients have been kept under observation. Only one has failed to attend since her discharge from hospital. The results of hæmorrhoidectomy may be assessed in three separate periods. In the period immediately following operation, pain, retention of urine, hæmorrhage, and occasionally incontinence of fæces may occur. The intermediate period, which lasts for about six weeks after leaving hospital, may be marred by delayed and faulty healing of the wounds which causes prolonged spasm, fissure-in-ano, and anal fibrosis. Late complications comprise stricture formation and recurrence of the hæmorrhoids; the latter cannot be assessed for many years.

The Period immediately following Operation.—In the operation of submucous hæmorrhoidectomy an attempt has been made to avoid pain by applying a high ligature which does not incorporate mucous membrane, by avoiding the use of tubes and packs, and by providing mucosal flaps to cover the denuded areas of the anal canal. Even so, this region of the body is so sensitive that it would be surprising if any incision into it, however small, were completely painless. Pain is also to be expected on stretching the wounded areas during the early bowel movements, or on any agitation such as intermittent sphincteric spasm. It is the universal experience of surgeons that the amount of pain following anal operations varies with the mental and emotional constitution of the patient. Tense, neurotic individuals have a great deal of sphincteric spasm; they experience more pain and are more liable to fibrosis and fissure than their more equable fellows. It is difficult to measure pain but a rough estimate may be obtained by two methods. The first is by noting the amount of morphine which the nursing staff regards the patient as requiring. The second is by witnessing his discomfort and by paying due regard to his complaints. In order to give a more precise expression to the latter method I have arbitrarily chosen six grades of post-operative pain. :—

0. No pain, but a little soreness with the first bowel action.

1. No pain except with the first bowel action.

2. Some soreness in the first two days, also with the first few bowel movements.

3. Soreness for the first few days with definite pain at the first bowel movement.

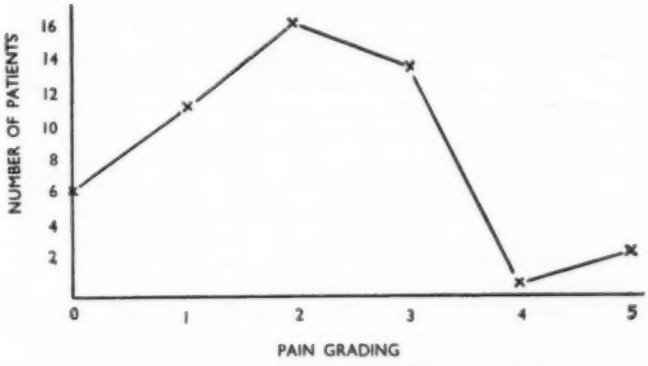

FIG. 396.—A graph to show the amount of pain suffered by the patients in the period immediately following operation.

4. The patient describes the operation as being painful.

5. The operation is accompanied by severe pain. The amount of pain suffered by my patients according to this method of assessment is shown in *Fig.* 396. The patients may be divided into three approximately equal groups. Those in the first group had no pain at all except with the first bowel movement. In the second group the only complaint was soreness for a few days. The remaining patients experienced definite pain occurring either spontaneously or with the first bowel movement. Two-thirds of the patients had no more than a few days soreness. Within twenty-four hours of the operation they were up for meals and toilet purposes. This, in my experience, is in marked contrast to those subjected to standard operations in which great discomfort occurs for at least three days. Only four of my patients had the degree of pain associated with other methods of hæmorrhoidectomy.

The series may also be divided into three equal groups according to the amount of sedatives given to each patient. Those in the first group required only codeine and aspirin to sleep at night and were comfortable during the day. In the second group one injection of morphine was needed to give restful sleep on the night of the operation. Of the remainder some received more morphine than they needed due to the nursing staff adhering to a routine customary when other methods are used.

Retention of urine occurs in those patients who have severe pain, especially in older men with

enlargement of the prostate gland. On two occasions only was carbachol necessary. One patient was an elderly man, the other a young man who was forbidden in error, to attempt micturition standing up. The small amount of pain which most of these patients experienced enabled them to get out of bed within a few hours of operation and as a result difficulties of micturition were reduced to a minimum.

Anal packs have not been used and a rectal tube was discarded after the first twenty-one patients had complained bitterly about it. Reactionary hæmorrhage was anticipated but did not occur. Bleeding has been less than that seen after standard hæmorrhoidal operations. Petit believed that the mucosal hood which covers the ligature and the flaps which meet over the muscle surface act as hæmostatic agents. This view is strongly supported by my own results. No reactionary or secondary hæmorrhage has occurred in any of the 50 patients of this series nor after the 50 operations performed subsequently.

Anderson (1909) commented on the loss of anal sensation and sphincteric control which may follow operations for hæmorrhoids, especially Whitehead's operation. Only 3 patients in this series had any disturbance of the mechanism of defæcation. The first and second were incontinent for five days, due mostly to an excess of liquid paraffin. The third complained of slight impairment of anal sensation for two months.

After this type of operation œdema rapidly approximates the edges of the skin wounds and they are healed within a week. Rectal examination performed on the fifth day reveals a remarkable absence of spasm. The ligatures can be detected high in the anal canal; ridges are felt where the two mucosal flaps of each wound come together. Patients are now allowed to go home a week after the operation; the average stay in hospital for the whole series was 8½ days. This compares favourably with the 21 days required in Anderson's series, but perhaps unfavourably with the practice of certain contemporary American surgeons who perform the operation at out-patient clinics.

On theoretical grounds we might expect submucous infection with abscess and fistula formation to follow this operation. Though acute infection of the hæmorrhoidal bed did occur in one case, no abscess or fistula has developed. The anal wounds heal with little or no pus formation.

The Intermediate Period.—The rectal and anal wounds are healed within two weeks. Proctoscopy performed three weeks after operation reveals simple linear scars. Anderson (1909) reported that the wounds of the ligature operation were not healed for a month at least. Complications in this period are due to delayed and faulty healing.

One complication peculiar to this operation is the cross union of mucosal flaps. This happened on one occasion and a bridge was formed across the anal canal which required excision. I believe this could have been avoided by more diligent rectal examination while the patient was in hospital.

The remaining evils which may ensue in this period are due to sphincteric spasm, which is largely dependent upon the emotional constitution of the patient. If spasm occurs in the period immediately following operation it delays healing of the wounds. Every bowel movement is painful and the healing surfaces are traumatized by the passage of each stool. This generates more spasm and if the vicious circle is not broken a chronic fissure-in-ano may develop. Though spasm is not common after this operation it occurred in varying degrees of severity in eleven patients. Technical faults accounted for its presence in over half this number. In one of them only was it severe enough to produce a fissure-in-ano which has healed with conservative treatment.

Spasm also leads to stenosis because fibrous tissue may be deposited in the wall of the spastic and contracted anal canal. Fear of pain may cause the patient to take so much liquid paraffin that liquid motions are produced and the anal canal is not dilated by the passage of a normal stool. If the patient allows the stools to become too hard the pain and trauma of each bowel movement cause more spasm and greater fibrous-tissue reaction.

In this series no case of anal stenosis has been seen. One patient was found to have a complete ring of fibrous tissue in the anal canal, but it allowed the passage of a proctoscope and disappeared in three months without treatment, dilated by action of the daily bowel movements. Another patient was found to have a semilunar fibrous deposit which was asymptomatic and required no treatment. No anal operation is free from the risk of submucous fibrosis; indeed one of the objects of the operation is to create a certain amount of submucous fibrosis. Some people show a greater tendency to form fibrous tissue than others and it is important that all patients should be observed until the wounds have healed. The few fibrous-tissue deposits seen after this operation have been localized and narrow. They have felt as though a purse string had been tied around part of the anal canal. It is now my practice to perform a digital examination weekly for three weeks after discharge from hospital; should early fibrous-tissue deposition be detected the patient is instructed to perform a daily digital dilatation. Only four of my patients have required this measure, compared with the 40 per cent in which Anderson reported it a necessity. An anal dilator was used by one patient only; he has already been mentioned because he developed a wound infection. Dilatation in this case was prophylactic; no stenosis occurred and the final result was excellent.

Technical faults are occasionally responsible for delayed healing. In a few of the more difficult cases the mucosal flaps were lacerated and left denuded muscle without epithelial covering. These patients had more pain and spasm than the others. Thread was used for ligation in some cases in the middle of the series. It caused delayed healing with the formation of granulating ulcers at the sites of ligation; it prolonged sphincteric spasm. In one patient the thread did not separate and had to be removed six months after operation. When submucous hæmorrhoidectomy is performed the ligatures are buried beneath the mucous membrane; it is wiser to use absorbable catgut than to risk the formation of submucous granulomata.

Late Complications.—As previously stated, anal stenosis has never occurred after this operation. It would be expected only after prolonged sepsis in the anal wounds.

The length of observation in the present investigation is inadequate to give any information as to the frequency of recurrent hæmorrhoids. Small symptom-less varices, remnants of secondary piles left behind at operation have been observed in six cases. Submucous injection of these hæmorrhoids is often impossible because the space has been obliterated by adhesion of mucosa to muscle. Injection directly into the varices will cause thrombosis.

It may be thought that 12 per cent is a high figure for the presence of residual varices. These cases occurred early in the series and increased experience has reduced their incidence. On occasions it has been thought wise to leave behind a secondary pile rather than risk undermining too much of the anal mucosa. I would like to make the point that the frequency with which residual varices occur after most hæmorrhoidal operations is unknown. These small venous dilatations are symptomless and are only detected by proctoscopy. They would have remained undiscovered had the after-care been such as the ordinary patient receives at the hands of an over-worked house surgeon. I would make a plea for the more careful observation of these patients after they have left hospital. If small remnants are treated by early injection they can be cured; untreated they may be the cause of recurrence of symptoms in later years.

The patients in this series have been observed very carefully and many of the undesirable features to which I have drawn attention would be passed by without comment after standard procedures. The impression gained from observation of these patients is that the trivial nature of the pain suffered, the rapid healing, the early mobility, and the ability to return to work within a short time have been ample reward for the work involved in evolving the method and giving it a thorough trial.

CONCLUSIONS

The anatomy of the anal canal has been the subject of fresh inquiry and certain new features have come to light. The mucosal attachment previously thought to be due to the insertion of an anal intermuscular septum has been shown to be due to a fibromuscular ligament connecting the mucosa of the anal crypts to the fibrous tissue on the internal sphincter. The internal sphincter forms the wall of the anal canal, the subcutaneous external sphincter is a relatively trivial muscle ring split up by the termination of the longitudinal muscle. The marginal or perianal space has been redefined.

Fresh views on the aetiology of hæmorrhoids are advanced. The view first proposed by Morgagni that the erect posture caused a high pressure in the superior hæmorrhoidal vein and that this resulted in the dilatation of the terminal venous plexus, has been discarded. It is thought that the true cause is to be found in the venous occlusion occurring during prolonged pelvic straining; the superior hæmorrhoidal artery fills the hæmorrhoidal plexus and distends the veins under a force equal to systemic arterial pressure.

On theoretical grounds the superior hæmorrhoidal artery should be ligated above the anorectal ring as in Salmon's operation. Modern authors advocate low ligation to avoid the formation of strictures which occur when much rectal mucosa has been removed. The operation described above combines the advantages of both methods; the superior hæmorrhoidal artery is ligated above the anorectal ring yet there is little loss of mucosa. The method also has the advantage that pain is slight, hæmorrhage very rare, and the patient returns to a normal life within 14 days of operation.

I am deeply indebted to many at Guy's Hospital for their help in the preparation of this paper. I am especially grateful to Mr. Grant Massie and Mr. Guy Blackburn for their permission to treat and report their cases; to Mr. H. J. B. Atkins in whose laboratory the anatomical research was performed; to Miss S. Treadgold, Mr. C. Engel and their staff for the illustrations. Above all I would like to thank Mr. S. H. Wass without whose constant advice and criticism this work would have been sadly incomplete.

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THE PATTERN OF OCCLUSION IN ATHEROMA OF THE LOWER LIMB ARTERIES

THE CORRELATION OF CLINICAL AND ARTERIOGRAPHIC FINDINGS

By G. E. MAVOR, Aberdeen

Atheroma with secondary thrombosis affects the arteries of the lower limb to a greater extent than elsewhere with the possible exception of the coronary system. The investigation and treatment of such cases of peripheral arterial disease has shown considerable advance in the last decade, and it is probable that much of this is due to the development of safe arteriography and its routine use. In this way a more precise understanding of the pathological basis of peripheral ischæmia secondary to atheroma has been obtained. Although it is recognized that occlusion may be segmental, less is known of the usual site and extent of such occlusion. By arteriography, apart from anatomical details, much can be learned about the localization of disease, and, by the correlation of clinical and arteriographic features, about the method of progression and accordingly the prognosis. These details acquire the greater importance with the recent advent of direct surgery for the occluded artery, for here the difficult question is always whether it is worthwhile to employ a local procedure in the treatment of a general condition. Such a decision must be made anew in each individual case, in the light of exact knowledge of the state of all the peripheral and visceral arteries, of the localization of disease and the stage of progression in the particular artery and its branches, and the prognosis as regards gangrene in the limb.

CLINICAL MATERIAL

This study is based on a series of 149 consecutive cases of atheroma with secondary thrombosis affecting the arteries of the leg seen over a period of six years in Aberdeen Royal Infirmary. Of these cases 124 had peripheral ischæmia without gangrene, and of these,

Table I.—Age and Sex Incidence in Atheroma with Secondary Thrombosis

Age in Years	*Cases*	
	Male	*Female*
21–30	1	—
31–40	9	—
41–50	28	—
51–60	59	4
61–70	27	7
71–	7	2

31 had evident bilateral disease, comprising 154 legs studied. The remaining 25 cases had early gangrene affecting the periphery and are included in an attempt to demonstrate the usual method of progression of the disease. They are considered separately. The age and sex incidence are shown in *Table I* (this excludes cases of gangrene). It is to be noted that this series does not represent an unselected group as over the period of the study there tended to be less reference of cases of established gangrene.

DIAGNOSIS

Besides complete clinical examination with urinalysis, blood Wassermann and Kahn tests, full blood-count, estimation of blood-urea, radiography of the chest and legs, and electrocardiography have been carried out in each case. Arteriography has been undertaken in every case, and the diagnosis is based on the clinical and arteriographic findings supported in every case by exploration and examination of the main artery of the limb, either femoral or popliteal, with occasional confirmation in difficult cases from histological examination of thrombosed arterial segments.

NOMENCLATURE

The term arteriosclerosis is used to describe changes which occur primarily in the medial coat of an artery. Pathologically, the lesion is a medial sclerosis, and in its severest form hyalinization and calcification occur. Thrombosis is not a feature of this diease, as the intima remains intact, so that the vessel remains patent, and even with advanced arteriosclerosis, there may be no peripheral vascular insufficiency. Atheroma or atherosclerosis is regarded as a distinct pathological entity where the principal findings are related to the intima, being in the nature of cholesterol and fatty acid formations. With such intimal damage, secondary thrombosis results and is regarded as the essential feature of the condition. The frequent association of the two conditions is not unexpected as atheroma is very common, and arteriosclerosis in some degree universal. It follows that when arteriosclerotic arteries become occluded, the process is begun as a result of atheroma and completed by thrombosis (Allen, Barker, and Hines, 1946).

CLASSIFICATION

Anatomically, atheroma may be divided conveniently into two groups, main vessel disease where it affects the iliæ, femoral, or popliteal arteries, and small vessel disease, where the anterior or posterior tibial or the arteries of the foot are the vessels involved. Clinically, there is some justification for such a division on the basis of both incidence and symptomatology. As regards the former in this series there are 111 cases of main vessel disease as opposed to only 13 cases of small vessel disease.

THE LOCALIZATION OF MAIN VESSEL THROMBOSIS

Atheroma in itself does not cause symptoms; sooner or later, however, secondary narrowing and then thrombosis supervenes, so that the main artery is occluded and symptoms arise. The onset of thrombosis may not be initiated entirely by the formation of an atheromatous plaque for, although this occurs, the possibility that the atheromatous vessel is more susceptible to the daily trauma of movement, muscle pull, and compression, has to be considered. The pathogenesis of atheroma is at the present time not clear, and what governs its localization in the arterial tree largely unknown. The latter

may be, however, in part related to mechanical factors. It is known that experimentally induced vitamin D sclerosis and cholesterol sclerosis do not occur together in the same location (Harrison, 1933), and it is thought that this may be due to the fact that the immobility produced in the artery by the one lesion renders the vessel less susceptible to the other. Lindbom (1950) is not alone in believing that the movement of vessels possibly determines the localization of human arterial disease. His radiological and pathological studies indicate that intimal thickening is most pronounced in two areas in the main vessel of the lower limb, at the adductor magnus opening area and just above the knee-joint (*Fig.* 397). There is at least anatomical evidence that at the former point

Table II.—SITE OF OCCLUSION IN 142 CASES OF CALF CLAUDICATION

Aortic bifurcation	4
External iliac artery	1
Femoral artery	104
Popliteal artery	16
Femoro-popliteal	14
Narrowing	3

the femoral artery is subjected to unusual stresses. Here it is securely anchored by the fascia of the adductor magnus, which blends with its adventitia (Mavor, 1952), and so anchored, it may not only be compressed, but angulated and dislocated by muscle contraction and pull from flexion and extension of the knee-joint (Lindbom). Just above the knee-joint, the popliteal artery is subject to similar though less severe trauma, so much so that its susceptibility to damage and thrombosis has been recognized (Boyd, 1938). During movements of the knee-joint, particularly extension, it may in its close relationship to the joint be exposed to angulation and stretching. Whether these factors play a role in the localization of atherosclerotic lesions remains extremely doubtful, particularly in view of the fact that atheroma may often be generalized in the arterial tree. It seems certain, however, that they are of great importance in the localization of secondary thrombosis. The very fact that atheroma is often generalized and thrombosis localized, suggests a local factor in the aetiology of the latter, and it seems likely that at the points under consideration, the adductor magnus opening area and just above the knee-joint, the mechanical stresses already described produce subintimal hæmorrhage in an already sclerotic and susceptible vessel. This produces further narrowing or total occlusion of the vessel and thrombosis supervenes. It is known that intimal bleeding is an important factor in the mechanism of coronary occlusion (Horn and Finklestein, 1940), while Lindbom has shown in post-mortem studies that it is a common pathological finding in the arteries of atherosclerotic patients, particularly in the lower extremities, where it is most marked at the adductor magnus opening area, just above the knee joint, and in the posterior tibial artery at ankle-joint level. These findings were so constant that he suggests that intimal hæmorrhage " may be regarded as an arterial disease in arteriosclerotic patients ".

It has been noted for some time (Leriche, 1946) that Hunter's canal is the usual site of occlusion, but that the thrombosis occurs so often (*Table II*) in this location is probably not realized. Excluding the cases of thrombosis above the inguinal ligament, and those of popliteal occlusion, in 121 out of 142 cases in the present series, the site of initial occlusion is in the femoral canal. The group of femoro-popliteal thrombosis does not constitute a separate group as these cases are regarded as evidence of further extension of a complete femoral artery thrombosis, thrombus propagation extending distally to the popliteal artery, so that the main vessel from profunda origin to popliteal termination is occluded.

SECONDARY FEMORAL THROMBOSIS

In 85 per cent of cases in the present series secondary thrombosis is located in the femoral artery. Further examination of these cases (*Table III*)

FIG. 397.—The upper two arrows indicate the site of the adductor magnus opening area. The lowest arrow shows the usual site of origin of secondary thrombosis in the popliteal artery, close to a constant and large muscle branch.

indicates that in all except two the site of origin of the thrombosis is at the adductor magnus opening area, for although short occlusions are common in the lower third of the femoral artery (*Figs.* 400–402), numbering 18, and in fact several arteries showed narrowing and very early thrombosis at this area (*Figs.* 398, 399), there are only two cases where the proximal superficial femoral artery is occluded without involvement of the distal. These figures indicate that thrombosis usually starts at the adductor magnus opening area and propagates proximally to reach in time the origin of the profunda femoris, so that when initially seen almost all cases will have thrombosed the superficial femoral artery in a varying extent distally (*Figs.* 403–406) or in its whole length (*Figs.* 407–410). The great importance of the profunda femoris as a main collateral is evident. This vessel is rarely thrombosed, a fact also noted by Lindbom, although Krahl, Pratt, Rousselot, and

Ruzicka (1954) report an incidence of thrombosis of 6 per cent in 50 cases. In 104 cases in the present series it was visualized, noted to be patent, and what is even more remarkable, free of disease. There is no known reason for the relative immunity of the profunda femoris, although it is interesting to speculate that in its course along the femur it may be splinted and thus protected from muscle action.

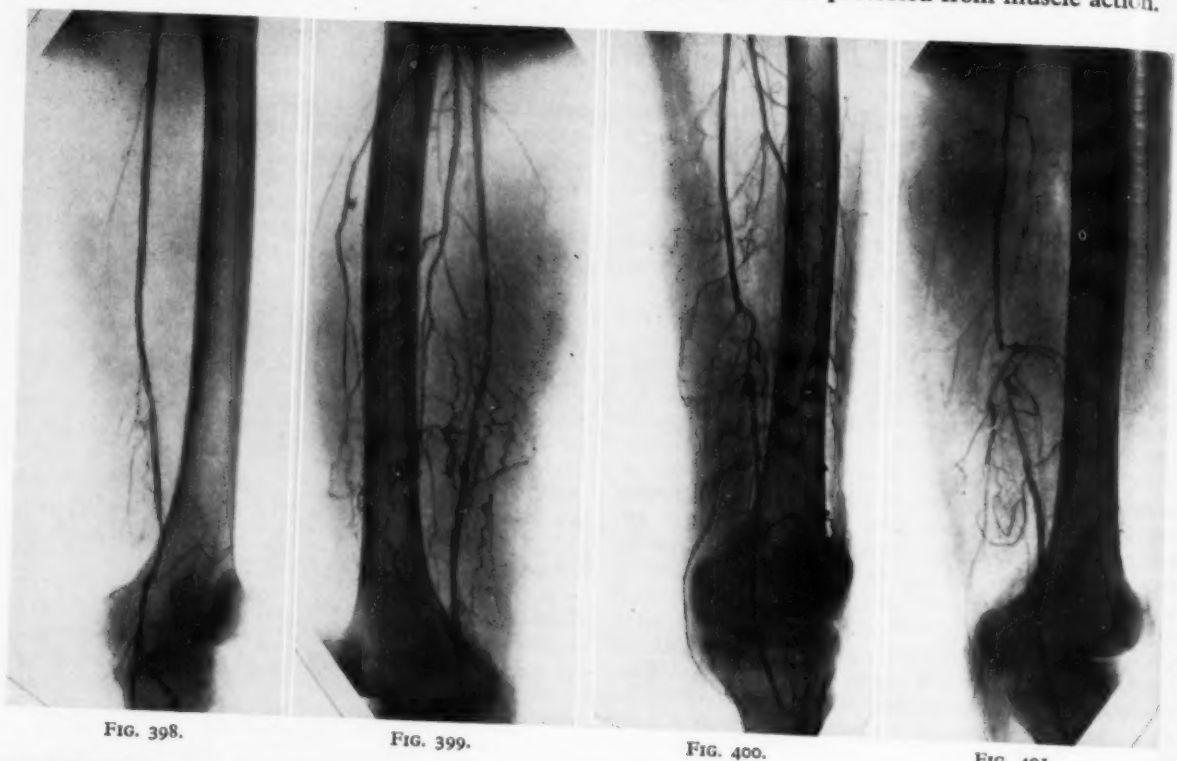


FIG. 398. FIG. 399. FIG. 400. FIG. 401.

FIG. 402. FIG. 403. FIG. 404. FIG. 405.

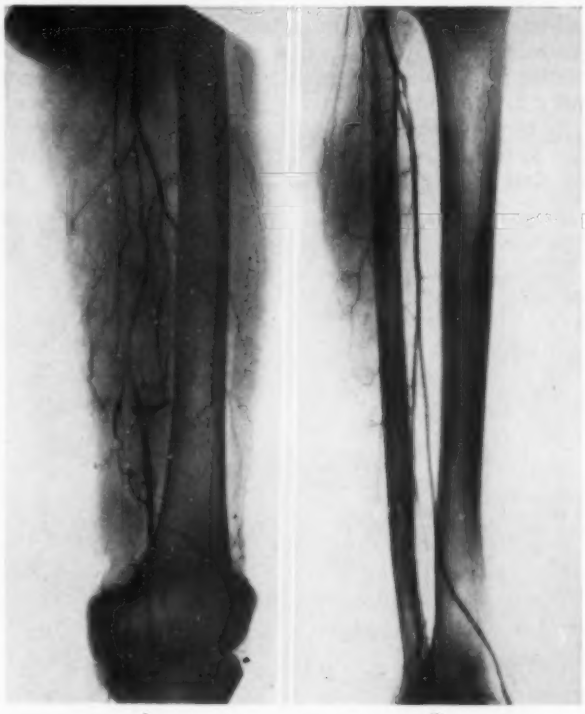
FIGS. 398, 399.—Narrowing and early thrombosis at the adductor magnus opening area.
FIGS. 400–402.—Short segmental thrombosis at the same area.
FIGS. 403–405.—Thrombosis of the lower third of the femoral artery. The rectus femoral collateral is seen in *Figs.* 403, 405.

SECONDARY POPLITEAL THROMBOSIS

The popliteal artery was the site of thrombosis in only 16 cases or 11 per cent. Five of these were short occlusions, and eleven long, involving the whole length of the artery or its distal part from the origin of the sural artery. The initial site of thrombosis is just above knee-joint level (*Fig.* 397) and short occlusions are seen only in this area (*Figs.* 411–413). Thereafter the thrombus may propagate proximally or much more commonly distally to the bifurcation of the popliteal artery, so that the whole popliteal becomes occluded (*Fig.* 414). In this series of 16, there was one unusual case (*Fig.* 415).

THE COLLATERAL CIRCULATION

It is the extent of the secondary thrombosis which determines the clinical manifestations of the disease. It is important to realize that the efficiency of the collateral circulation depends on the level to which it can refill the main stem artery (Learmonth, 1944). A good collateral circulation means that the thrombosed segment will be short, or put in another way, the shorter the thrombosed segment, the better and freer the collateral circulation. The extent of the block depends on several factors—the age of the patient, the anatomy of the arterial tree, the suddenness or otherwise of the main vessel occlusion, the speed of development of the collateral circulation, and finally the presence of, and if present the degree of, arteriosclerosis. These factors are interdependent. It is worth noting that apart from odd instances where it may in small vessels produce an endarteritis with occlusion, this is the most significant way in which arteriosclerosis influences the development of peripheral vascular insufficiency. Should the arterial tree be grossly arteriosclerotic, then the development of the collateral circulation will be seriously handicapped.



A B

FIG. 406.—A, Thrombosis of the lower half of the superficial femoral artery. B, The critical part played in the collateral circulation by the last perforating artery is shown. The profunda branches are widely concerned in the anastomosis. The popliteal is patent and healthy, as are the lower leg vessels.

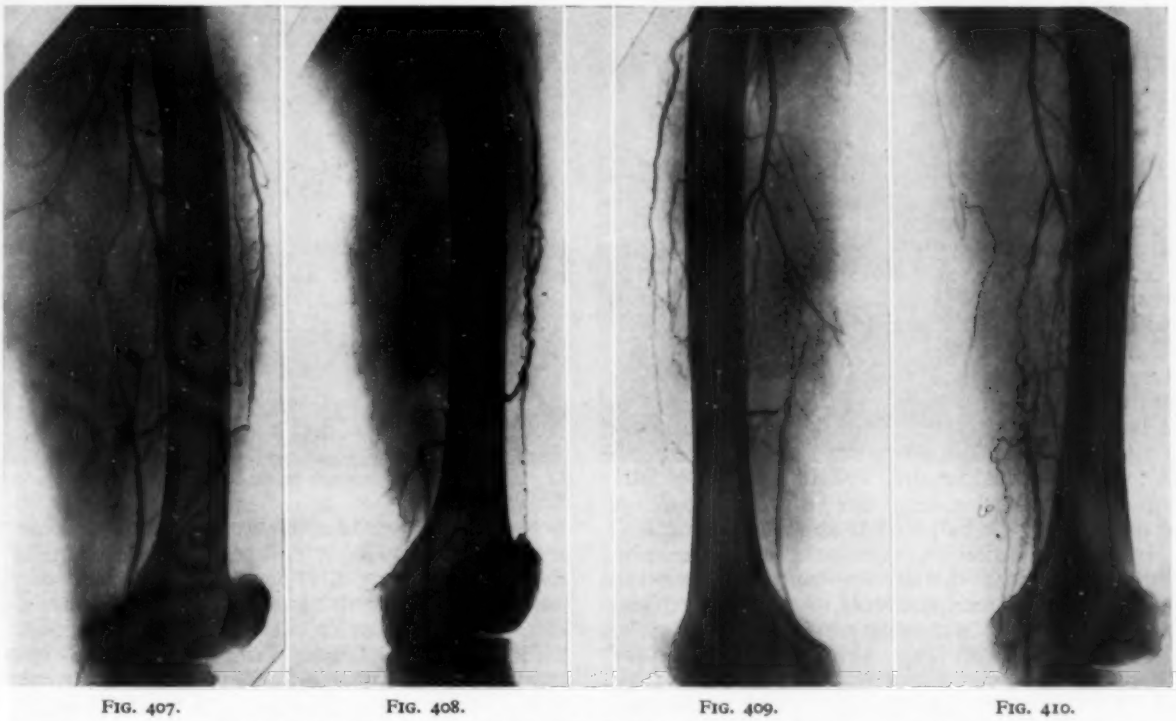


FIG. 407. FIG. 408. FIG. 409. FIG. 410.

FIGS. 407–410.—Thrombosis of the femoral artery from profunda origin to the adductor magnus opening. The importance of the rectus femoris collateral and of the last perforating artery is evident.

The secondary thrombosis will propagate in both directions up to the first collateral of any consequence. Thrombosis in the femoral artery is limited proximally by the profunda femoris, while more distally at the adductor magnus opening area a constant muscle vessel to the vastus medialis, which may be either a deep branch of the descending genicular or may arise from the parent stem, has an important role to play (*Fig.* 397). This vessel initially prevents the spread of a femoral thrombosis to the popliteal, so that in the first instance from its origin at the adductor magnus opening area a femoral thrombus will propagate proximally. The comparative absence of branches in the proximal superficial femoral artery gives an anatomical explanation for this proximal propagation, for with a distal block the blood-flow will be very slow in the patent proximal segment of artery. The collateral vessels are mainly derived from the profunda femoris system and in particular the last perforating artery usually has a critical part to play in the final anastomosis (*Figs.* 406 A, 407–410). The rectus femoris collateral is also fairly constant, may reach a large size (*Figs.* 405, 408) and can occasionally be palpated as an abnormal pulse.

In popliteal occlusion propagation of the thrombus generally proceeds distally in contradistinction to thrombosis in the femoral artery. Again an explanation is forthcoming in the relative absence of branches in the distal popliteal (*Figs.* 397, 410, 412, 413, 415) in contrast to the proximal part of the artery (*Figs.* 412, 413, 415). Here initially a fairly constant muscle branch (*Fig.* 397) limits extension. Eventually, however, the whole popliteal becomes occluded and then the barriers to further extension are the muscle branch to vastus medialis already mentioned, and distally the recurrent genicular arteries from anterior and posterior tibial vessels. Although with progression, a femoral thrombosis may propagate distally into the popliteal, there is no evidence in this study to suggest that the reverse occurs.

The localization of branches in the adjacent lower part of femoral and upper part of popliteal arteries has an important influence on limiting thrombus propagation. Occlusion proximal to this branch-bearing area may remain local for some time as the proximal femoral and profunda femoris branches have the means of free anastomoses with distal femoral and proximal popliteal branches. When, however, the popliteal is thrombosed, not only are many of the available collateral vessels occluded at their origin, but the distal anastomoses depend entirely on the small recurrent genicular vessels, the distal popliteal being devoid of branches. It is evident that a femoral thrombosis may remain localized for some time, while a popliteal thrombosis has a much worse prognosis, as distal propagation into the lower leg arteries is likely to occur at an early date.

FIG. 411. FIG. 412. FIG. 413. FIG. 414.

FIGS. 411–414.—Secondary thrombosis of the popliteal artery. *Figs.* 411, 412 illustrate the initial site of thrombosis. *Figs.* 413, 414 show the important descending genicular collateral. Although the main vessel looks healthy, the 'pinched' origins of its branches is typical of atheroma.

Table III.—EXTENT OF FEMORAL ARTERY OCCLUSION

Upper third	1
Upper two-thirds	1
Lower two-thirds	56
Lower third	18
Whole femoral	28

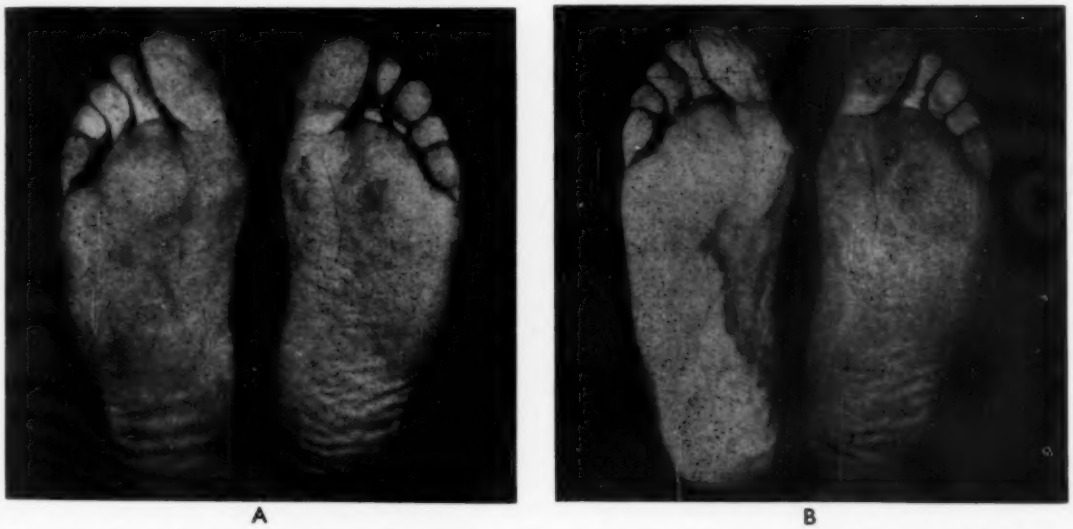
The term 'femoral artery' refers to the superficial femoral artery, i.e., the vessel from profunda origin to the opening in the adductor magnus.

THE CLINICAL FEATURES

It has been recognized for a long time that calf claudication is the classic symptom of main vessel thrombosis (Bouley, 1831, Brodie, 1846). Furthermore where there is no nutritional upset of the limb at rest, and certainly no question of gangrene, it is almost invariably the case that when the femoral artery is thrombosed, the popliteal artery is patent, and when the popliteal is blocked, the femoral is free of thrombus. Only under these conditions of limited main vessel thrombosis does the collateral circulation, using all available channels, achieve an adequate by-pass function (Learmonth, Blackwood, and Richards, 1944). The main stem artery is then refilled at a high level, thereby restoring circulatory normality as proximally as possible, and limiting the functional disability of the limb to periods of exercise. Calf claudication may also arise from narrowing of the main artery, according to Lindbom (1950) when its lumen reaches 20 per cent of normal. Three cases are noted in the present series (*Table II*). This is only a transient phase, and with such narrowing, secondary thrombosis cannot be long delayed. Apart from main vessel narrowing and thrombosis, calf claudication has not been noted, and no evidence has been found in this series that it is present in disease of the calf muscle vessels only without main vessel occlusion, as has been stated elsewhere (Kinmonth, 1948; Annot. *Brit. Med. J.* 1952).

It is well known that this symptom of calf claudication is by no means a constant one. Its exact nature and severity varies from patient to patient, and in an endeavour to standardize patients, Boyd, Ratcliffe, Jepson, and James (1949) classified their cases into three groups, depending on the effect of continued exercise on the pain. In Group 1, the pain disappeared if exercise was continued; in Group 2, the pain maintained a steady level; and in Group 3, the pain gradually increased in severity until it halted the patient. They considered that these three clinical groups in fact related to varying degrees of arterial insufficiency, presumably in all there being some interference with main vessel flow. Group 1 cases were least affected, whereas in Group 3 the main vessel disturbance was considerable. In this series of 142 cases of calf claudication, no case has been noted where further exercise produced either alleviation or disappearance of the pain. A similar report comes from Hamilton and Wilson (1952). There is no evidence that Group 3 type of calf claudication was related to a constantly marked degree of peripheral vascular insufficiency. Many cases had a very short main vessel thrombosis, which is usually accepted as the best evidence of a well developed collateral circulation. The following case is typical.

FIG. 415.—A short area of thrombosis just proximal to the popliteal bifurcation.



A B

FIG. 416.—Secondary thrombosis affecting the femoral artery. A, Shows the feet at rest; B, Illustrates typical pallor of the plantar aspect of the right foot, seen after exercise. Pulp atrophy of the right great toe is conspicuous.

Case 92.—W. M., aged 72 years, had Group 3 type claudication pain with an exercise tolerance of approximately 250 yards. The pain was of twelve months' duration. There was no evidence of ischæmia at rest. Arteriography revealed a short lower third femoral artery thrombosis, and no disease below the knee. Furthermore, the skin temperature recordings over the toes after heating the trunk showed a rise from 19·6° to nearly complete vasodilatation at 32°.

It is of further interest to note that not only may leg pain vary from patient to patient, where the length of the main vessel thrombosis is practically identical, but it may also vary noticeably in any particular patient, frequently from day to day, often from season to season. Calf exercise pain can be influenced by treatment methods which could not possibly benefit the local condition. In the majority of cases in this series bed rest has had little effect on exercise tolerance. Occasionally, however, and without apparent reason, there has been a great increase in exercise tolerance as a result of bed rest in hospital. These general observations serve to stress the fact that it is unsatisfactory to use calf claudication in any way as an index of peripheral muscle ischæmia, as the symptom is totally unreliable, or to use exercise tolerance as a yardstick in assessing any form of treatment, whether this exercise tolerance test is carried out under as natural conditions as possible, or with the aid of an artificial manœuvre or machine (Boyd, Ratcliffe, Jepson, and James, 1949; Shepherd, 1950; Hamilton and Wilson, 1952).

In the majority of cases the onset of thrombosis is a gradual process and the collateral circulation, under the stimulus of peripheral ischæmia, is given time to develop. Under these circumstances, the complaint of typical cramp-like exercise pain is often preceded for some days or perhaps weeks, by tiredness and tightness in the calf. In 9 per cent of cases in this series, however, the episode of thrombosis is sudden, and acute symptoms resembling those of peripheral arterial embolism are present. The prognosis is adversely affected for the collateral circulation has little time to develop, so that an extensive main vessel thrombosis is a likely event from the outset. That this is in fact thrombotic and not embolic is suggested by the localization of occlusion.

The incidence of coronary occlusion in this series is 12 per cent. This figure is based on electrocardiographic evidence. In 14 cases with a definite history, the onset of calf claudication was antedated by the myocardial infarction in 11.

Case 141.—J. A., aged 58 years, had right calf claudication for about one year. Just prior to the onset he had spent six weeks in bed at home with a suspected coronary occlusion. After he was allowed up to walk, he noted calf exercise pain. An electrocardiogram showed evidence of an old posterior infarct.

It seems likely that with atheroma of the main limb artery and narrowing already present, the slowing of the peripheral blood-flow due to diminished cardiac output and hypotension resulted in complete blockage of the artery.

Although calf claudication may be the only symptom of peripheral ischæmia, usually there are others. Muscle wasting and hypotonia should always be looked for. More common are the complaints of coldness and pallor, nearly always referable to the foot of the affected leg. These complaints are more marked during and after exercise, when a greater proportion of the available blood-flow, limited already by main vessel thrombosis, is diverted from skin to active muscle. In this way the skin suffers relative ischæmia and becomes pale and cold. The coldness may be intense, almost to the point of numbness, and occasionally it is the main complaint. The pallor is often striking, the whole foot becoming deathly pale. It is always worth while examining the feet of a patient with peripheral vascular insufficiency after exercise. Pallor may be definite or may be limited to the plantar aspect of the foot of the affected leg or to the toes (*Fig.* 416). If it is detected, its occurrence is always significant. In this series exercise tests for pallor revealed its presence in 76 per cent of cases. There is no evidence to suggest that arterial spasm is of frequent occurrence in the vessels of these limbs, and it would seem certain that this exercise pallor is not due to spasm, as in many cases it has been noted after adequate sympathectomy.

The peripheral pulses are important. Absence or delay in the femoral pulse is indicative of arterial obstruction above the inguinal ligament. A thrill or bruit just below the ligament often indicates thrombosis of the main artery up to the origin of the profunda femoris. It is a general rule that no case of calf claudication has a palpable popliteal pulse. However free the collateral circulation in cases of femoral thrombosis, it is never free enough to restore the pulse-wave to the popliteal artery, although very infrequently it may return it to the arteries at the ankle. Nevertheless, occasionally in a patient with a typical history, the popliteal pulse may be palpable, the explanation being that the point of palpation, against the lower femoral shaft, is proximal to the site of the thrombosis. Generally, then, in most cases all pulses distal to the femoral are absent. In this series, the posterior tibial pulse has been noted in 5 legs, the anterior tibial in 1, and both pulses have been palpated on 2 occasions. Sometimes an abnormal pulse, which is due to a particularly large collateral vessel, may be palpated. The three commonest are the rectus femoris collateral (*Fig.* 408), the sural collateral felt superficially and sometimes visible in the popliteal fossa (*Figs.* 412, 415), and the anastomotica magna or descending genicular artery (*Fig.* 414) palpated on the anteromedial aspect of the lower thigh just above the condyle of the femur and behind the sartorius. Needless to say the whole thigh and knee region should be palpated for an abnormal pulse.

COMMENT

It is worth noting that as regards the incidence of secondary femoral and popliteal thrombosis, these findings (*Table II*) agree with those of Lindbom, but conflict with those of Boyd, Ratcliffe, Jepson and James, who state that "thrombosis of the superficial femoral artery is much less frequent" (than secondary popliteal thrombosis), occurring in "only 55 out of 472 patients", while popliteal thrombosis occurred in nearly half the cases, presumably over 200.

It is probably not generally recognized that such a large proportion of cases out of a series of patients

with calf claudication has a comparatively short main vessel thrombosis. Excepting the cases of femoro-popliteal thrombosis, in 88 per cent of cases the thrombosis is of limited extent, and conceivably amenable to some method of surgical reconstruction,

Table IV.—MAIN VESSEL OCCLUSION: INCIDENCE OF ASSOCIATED OCCLUSION IN THE LOWER LIMB ARTERIES

Main vessel occlusion	147
Small vessel occlusion	
i. Adequately visualized	140
ii. No occlusion	106
iii. Occlusion without symptoms	27
iv. Occlusion with symptoms	7

whether by direct replacement of the occluded segment or by the employment of a shunt arterial homograft in order to preserve collateral channels. But in this group of 125 cases there are definite contra-indications to surgery. In 18 cases there is evidence of coronary disease, and in these apart from the grave risk of surgery, the leg exercise pain is considered a useful brake on physical activity, and as such no interference is thought justifiable. In 11 the thrombosis, popliteal in origin, extends to the bifurcation of the artery, making the task of distal anastomosis too hazardous to warrant the attempt. In a further 11 cases, evidence of atheroma is so generalized both in the main vessel and in the lower leg, where the local thromboses are present without added symptoms, as to preclude a main vessel procedure. It is, however, doubtful as yet whether the latter is a justifiable argument against a palliative procedure on the main vessel, because if successful the increase in blood-flow resulting would undoubtedly improve the prognosis by delaying further distal thrombosis. Excluding these cases, it is possible that of the original 142 patients, 85 or 59 per cent could be justifiably subjected to local palliative surgery.

In these cases of main vessel thrombosis the vessels of the lower leg are usually healthy (*Figs.* 406 B, 421 B). In 140 cases in which the lower limb arteries were adequately visualized, 106 or 76 per cent were free of disease (*Table IV*). In the remainder, the presence of localized thromboses did not in the majority of cases affect the clinical picture (*Table IV*). When it did and a more marked degree of peripheral vascular insufficiency was noted, this usually manifested itself by the development of rest pain in the foot and by failing skin nutrition.

FEMORO-POPLITEAL THROMBOSIS

Femoro-popliteal thrombosis is considered as a separate group as it represents the stage of failure of the collateral circulation in that clinical deterioration becomes obvious, and peripheral ischæmia develops to such a degree as to produce symptoms at rest.

In the main vessel thrombus propagation is the usual method of progression of the disease, and this usually occurs from femoral to popliteal locations as arteriograms at the femoro-popliteal stage show the remains of a proximal or femoral occlusion type of collateral circulation (*Figs.* 417–421 A) and often a short patent distal portion of the popliteal artery (*Figs.* 417, 420), which inevitably becomes thrombosed. There is no evidence in this study that propagation occurs from popliteal to femoral, although the series of popliteal occlusions is small. With popliteal thrombosis, propagation occurs distally into the lower leg vessels.

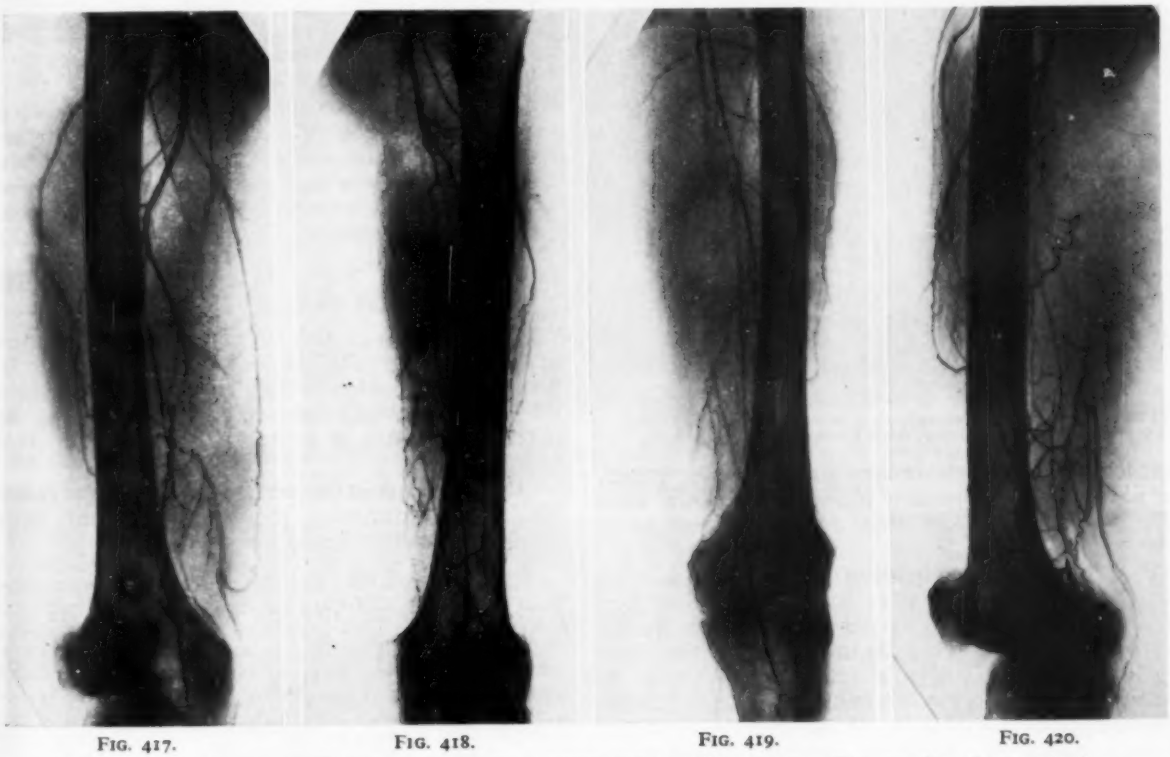
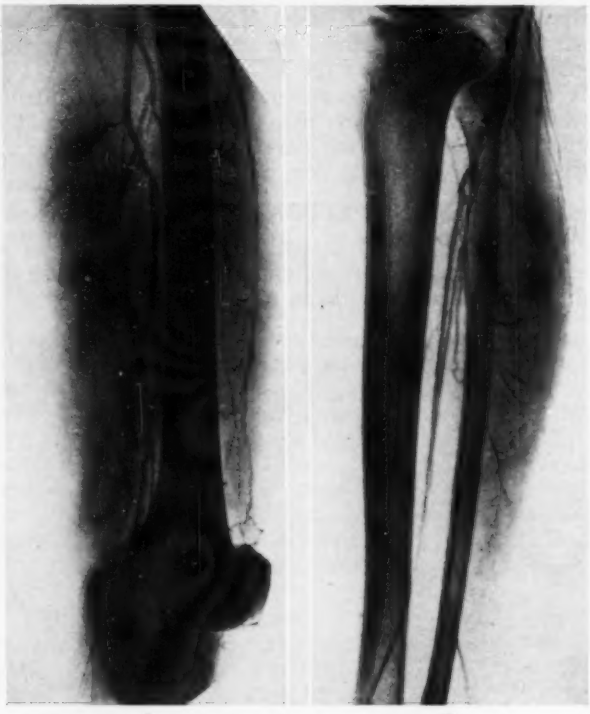


FIG. 417. FIG. 418. FIG. 419. FIG. 420.

FIGS. 417–420.—Femoro-popliteal thrombosis with a patent distal popliteal artery. The remains of a proximal or femoral occlusion type of collateral circulation are evident.

Besides thrombus propagation, progression may occur by the development of thrombosis at a fresh site in the main artery. In this way a segment of main artery remains patent for a short time (*Figs.* 402, 420). This is not common, being noted only in six cases in this study or 4·2 per cent. When such



A B

FIG. 421.—A, B, Femoro-popliteal artery thrombosis. The profunda femoris is healthy, as are the vessels below the knee.

multilocular occlusion occurs in the main vessel, the presence of a patent segment does not alter to any extent the expected degree of peripheral ischæmia.

The collateral circulation in these cases of femoro-popliteal thromboses has failed in that it is no longer acting as a by-pass. The main vessel thrombosis is extensive, the nutrition of the limb depends on the collateral circulation which is inadequate for such a function. Further clinical deterioration is inevitable, taking the form pathologically either of extension into the lower limb arteries or of multilocular thromboses in them. Lindbom believes that the latter is the usual method of progression, and this would seem probable in the presence of atheroma in the lower limb arteries, noted to be commoner in the older age groups. In the majority of cases with main vessel occlusion, however, the lower limb arteries are at first healthy (*Table IV*), and, if they remain so, progression occurs by propagation.

Clinical Features.—Clinically, these patients with femoro-popliteal thromboses have suffered from calf claudication for years, but now with the progression of the thrombosis, rest pain becomes their chief complaint. Rest pain precedes or accompanies gangrene, and is generally associated with skin changes in the foot (*Table V*). It is classically a burning pain, situated in the foot, most severe at night, and is influenced by temperature and by the posture of the limb (Paterson Ross, 1944). The affected parts are discoloured, erythematous, and cyanotic, often hyperæsthetic and usually cold. The patchy involvement of the skin of the foot is not so much due to scattered involvement in disease of small skin vessels, although local thrombosis may play a role in precipitating gangrene, but rather is prolonged irregular ischæmia which occurs mainly after exercise in association with the extensive main vessel thrombosis. The prognosis is grave when rest pain is present, and there must always be the possibility of gangrene developing at any time. The extending

Table V.—CORRELATION OF EXTENT OF THROMBOSIS WITH MAIN SYMPTOM AND THE PRESENCE OR ABSENCE OF SKIN CHANGES

Extent of Thrombosis		*Main Symptom*		*Skin Changes*	
Femoral artery	104	Calf claudication	104	Absent	104
Popliteal artery	16	Calf claudication	16	Absent	14
				Present	2
Femoro-popliteal	34	Calf claudication	14	Absent	1
		Rest pain	20	Present	33

thrombus, which can now spread into the lower leg vessels, has blocked off collateral after collateral until the nutrition of the skin and of the limb itself is in the balance. This balance is very often adversely affected by mild trauma, such as may result from a visit to the chiropodist, or by local infection.

SECONDARY THROMBOSIS ABOVE THE INGUINAL LIGAMENT

In this series there have been five cases of arterial occlusion above the inguinal ligament. This is a much lower incidence than that recently suggested by Kekwick, McDonald, and Semple (1952), who noted 8 cases out of 53 cases of intermittent claudication studied.

Of the 5 cases in this series, 1 was a case of external iliac artery thrombosis, the 4 other patients having aortic bifurcation thromboses.

Case 131.—A. W., aged 61 years, when first seen in 1948, had left calf claudication with a palpable left femoral pulse. This was equal and synchronous with the femoral pulse of the right side, where all the peripheral pulses were noted to be present. A left lumbar ganglionectomy was carried out. One year later in 1949, his condition had improved considerably in regard to the left calf exercise pain.

In 1950 it was noted that right calf claudication was his main complaint. Both femoral arteries were easily palpable and equal. There was no thigh pain. A right femoral arteriogram showed a long femoral artery thrombosis.

In 1951 he had an episode of sudden pain in the right thigh, and shortly afterwards the right femoral pulse was noted to be absent. A right lumbar ganglionectomy was carried out. It was considered that an extension of the right femoral thrombosis had occurred in a proximal direction.

Seen later in 1952, no peripheral pulses were noted. The femoral arteries on either side could be palpated as hard, thrombosed cords. Rest pain was his main complaint, and the left foot was grossly ischæmic, the skin being reddened and atrophic.

Summary of the case. It was considered that this patient had had a bilateral main vessel thrombosis, presumably femoral in extent, which had extended proximally, eventually reaching the aortic bifurcation.

CLINICAL FEATURES

The clinical features of these cases with arterial obstruction above the inguinal ligament have been recently described (Kekwick, MacDonald, and Semple, 1952; Burt, Learmonth, and Richards, 1952). *Case* 131 is of interest as the clinical history indicates that the thrombosis began in the femoral by Kekwick, MacDonald, and Semple It may have a higher incidence than this, as seen at a late stage it is difficult to ascertain the site of onset and the direction of main propagation of the thrombus.

Comment.—As Kekwick, MacDonald, and Semple mention the possibility of surgery for these cases, and suggest that therefore " accurate

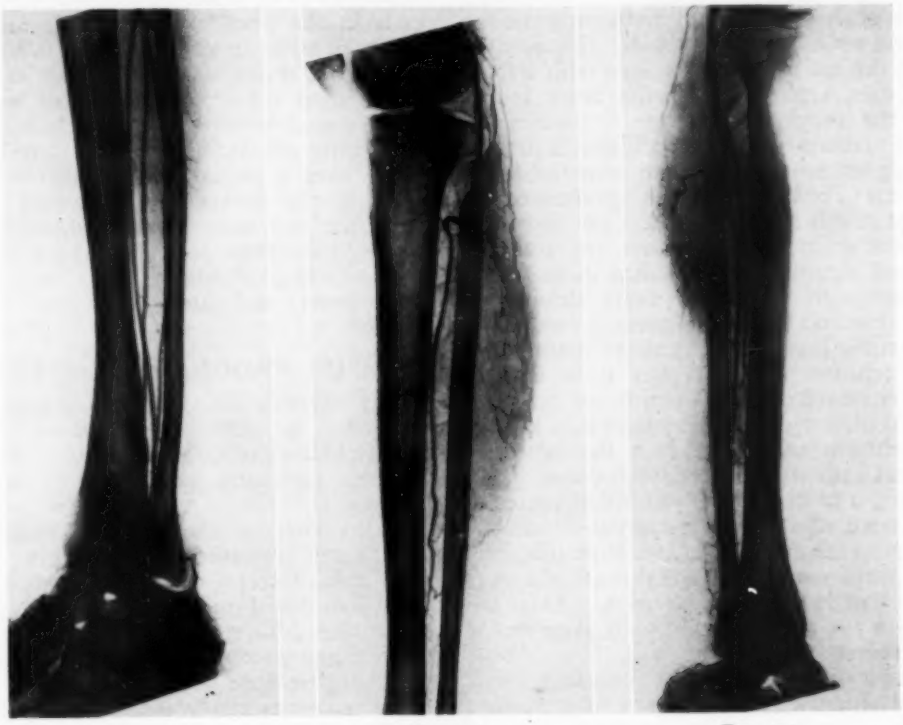
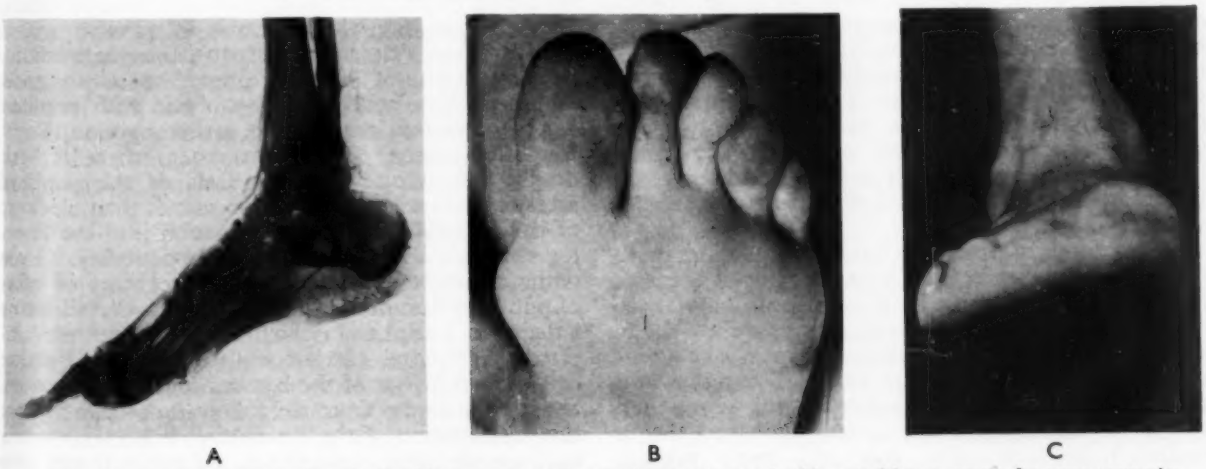


FIG. 422. FIG. 423. FIG. 424.

FIG. 422.—Thrombosis of the posterior tibial artery on the medial side of the os calcis. Elsewhere the lower leg vessels appear healthy.
FIG. 423.—Thrombosis of the posterior tibial artery at its origin. There is no distal filling of the vessel.
FIG. 424.— Distal thrombosis of the anterior and posterior tibial arteries.



A B C

FIG. 425.—A, Digital artery thrombosis with gangrene. The arteriogram shows a healthy arterial tree, except for some tortuosity of the vessels, but no visualization of the digital arteries suggesting thrombosis. B, Shows the four gangrenous toes, which were amputated along with the healthy third toe. C, The wound healed normally.

arteries and extended upwards to produce a clinical picture indistinguishable from an aortic bifurcation thrombosis. This is not an uncommon sequence of events, occuring in 2 out of the 11 cases of aortic thrombosis reported by Burt, Learmonth, and Richards, and in probably 1 of the 11 cases recorded location of the site of arterial obstruction is increasingly important ", it is pertinent to note that the presence of distal extension of the thrombus bilaterally into the femoral arteries in part or in their whole lengths, will probably preclude surgery, certainly of the endarterectomy type. In other words

if the answer is to be provided by surgery at all, then diagnosis with arteriography at an early stage in the disease is an essential preliminary. This is the lesson particularly underlined by those cases where there has been mainly proximal propagation of the thrombus.

SMALL VESSEL DISEASE

The vessels of the lower leg are frequently the site of atheroma and secondary thrombosis. Usually the localization of disease here is associated with a main vessel thrombosis, although with the latter lesion, occlusion in the lower leg arteries is uncommon (*Table IV*). Furthermore, when occlusion is present in the lower leg arteries, it is seldom responsible for added symptoms (*Table IV*), and its significance lies in the fact that it will materially affect the degree of peripheral vascular insufficiency once the stage of femoro-popliteal thrombosis is reached in the main vessel. In fact with femoro-popliteal thrombosis and lower leg vessel occlusion, gangrene is inevitable. In this study in the presence of localized main vessel thrombosis, occlusion in the lower limb arteries producing an increased degree of peripheral ischæmia has occurred in only 7 cases or 5 per cent. In 5 of these, the occlusion was located in the posterior tibial artery and caused foot exercise and rest pain ; in the remaining 2 cases, both anterior and posterior tibial arteries were affected and gangrene resulted.

Occasionally in the presence of extensive atheroma affecting the whole arterial tree, thrombosis may commence in the lower limb arteries. This has occurred once in the present series with gangrene as the inevitable result.

There remains the third group of cases with lower leg artery involvement as the initial site of occlusion. Atheroma with occlusion and symptoms presenting here is uncommon, only 13 cases being noted in this series. The localization of occlusion has no characteristic distribution below the knee as it has above, although in all 9 cases the posterior tibial was involved whether in part or in its whole length (*Figs.* 422, 423), there being an associated occlusion of the anterior tibial in 3 (*Fig.* 424). The cases of digital thrombosis (*Fig.* 425) form a small but important group with the interesting low age average of 57 years. These figures do not include any case of diabetes, in which atheroma characteristically affects the smaller vessels.

This total of thirteen cases of atheroma with occlusion in the lower limb arteries is not an accurate indication of incidence, as it represents only those cases with symptoms, and to produce these, as Lindbom noted, " occlusion must be pronounced ". In fact all the cases of anterior and posterior tibial artery occlusion in this group had extensive thrombosis, the artery involved being occluded in continuity and no distal portion being visualized. Localized thromboses in the lower leg arteries do not produce symptoms.

Clinical Features.—In the presence of occlusion of the anterior and posterior tibial arteries, the collateral circulation maintains a blood-flow through the plantar and digital arteries adequate for the nutrition of the forefoot and toes (Paterson Ross, 1944), so that gangrene does not often occur, except in the presence of complicating circumstances such as uncontrollable infection in a diabetic patient, and the resting requirements of the limb are met, symptoms being related to periods of exercise. Extensive secondary thrombosis of the anterior tibial artery gives rise to exercise pain in the anterior tibial compartment, while posterior tibial artery involvement produces either low calf claudication if the occlusion is at the origin of the vessel, or exercise pain in the small vessels of the foot if the distal posterior tibial or lateral plantar is blocked.

Digital thrombosis may occur in a younger age group than other cases of small vessel atheroma. Such digital involvement is seldom isolated, several toes being affected either simultaneously or successively over a period. This was found in all four cases in this series, the illustrated case (*Fig.* 425) being the one most extensively involved. Gangrene is the inevitable and immediate result, but the prognosis is good as there is no proximal disease of the vessels, and local amputation is followed by healing.

THE PROGNOSIS IN ATHEROMA

As regards the leg, the overall prognosis in atheroma is difficult to assess. It is related mainly to the collateral circulation, which in its turn depends on many factors, which have been duly noted.

The site of the initial thrombosis and its subsequent extension are largely dependent on anatomical factors, which are likely to be constant. The anatomical requirements of a good collateral circulation indicate that a femoral thrombosis will show a greater tendency to remain localized than a popliteal, because in the case of the former, many distal anastomotic vessels are available and the popliteal artery is patent, so that the thrombus has little chance of propagating distally in the initial phase. Under these circumstances with the blood returning to the main vessel with little loss of volume flow and reaching the arterioles in quantity and at high pressure (Learmonth, 1950), the prognosis for the nutrition of the threatened part is good. Although these conditions also obtain with popliteal artery occlusion, contrary to earlier opinion (Boyd, Ratcliffe, Jepson, and James, 1949) there is little doubt that secondary thrombosis of the popliteal artery carries with it a worse prognosis than blockage of the femoral, as distal propagation into the lower leg vessels is always an immediate possibility. Even without such extension a small percentage of cases of popliteal thrombosis show skin changes, indicating a degree of peripheral ischæmia which is not encountered in femoral thrombosis (*Table V*). Further evidence in favour of the better prognosis of femoral thrombosis comes from the follow-up of cases where the initial extent of the thrombosis is known. Over the past six years, 1 case of femoral artery thrombosis out of 104 seen, has progressed to gangrene, while of the 16 cases of popliteal thrombosis, 2 have deteriorated to this extent, necessitating amputation.

It is also noted that the speed with which the initial thrombotic episode occurs has a direct bearing on the collateral circulation, on the length of the initial thrombosis, and consequently on the prognosis. Of the 13 cases with a sudden occlusion, only 2 have a limited thrombosis, while the others when first seen

had a femoro-popliteal thrombosis, and 2 of these cases progressed to gangrene in an unusually early age group (52 and 53 years of age).

Besides giving information about the site and extent of thrombosis, arteriography can indicate the extent of atheroma in the main vessel, and also whether or not there is disease below the knee. The former, when present will hasten the development of a femoro-popliteal thrombosis, while the latter, when extensive, will not materially effect the prognosis until this stage is reached. From experience it seems likely that once the stage of femoro-popliteal thrombosis is reached, gangrene is inevitable and usually develops within a few months. There are, however, occasional exceptions to this general rule, the significant finding in such cases being a completely healthy arterial tree below the knee. Without the latter this ominous prognosis is related in the last resort to the nature of the collateral circulation. This is of the type where the periphery depends for its nutrition on terminal branches, and no part of the main arteries is refilled distally. Under these circumstances, there is great loss of volume flow in the collateral branches, low peripheral blood-pressure, and absence of distal pulsation (Learmonth).

Small vessel occlusion must be extensive even to produce symptoms on exercise and at rest. However, repeated trauma or persistent local infection such as occurs in diabetics will adversely affect the prognosis in these cases. With the aid of antibiotics and in the absence of diabetes local infection can usually be overcome, and healing will follow local amputation for gangrene. However, in diabetics, local wounds do not heal, and although the arterial disease may not involve the main vessel, infection usually demands major amputation, which, however, can be limited.

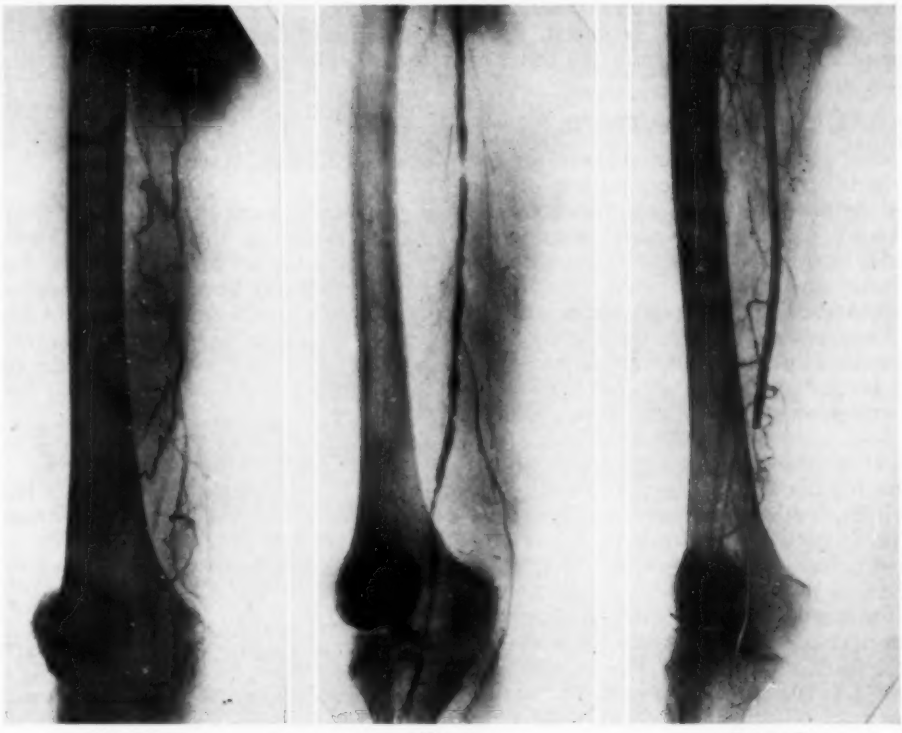


FIG. 426. FIG. 427. FIG. 428.

FIG. 426.—A diseased proximal stump of the femoral artery and the remains of a collateral circulation.
FIG. 427.—Extensive changes in the main vessel, thrombosis of which will quickly become consecutive and lead to extensive gangrene.
FIG. 428.—The typical picture of popliteal embolism. There is no collateral circulation.

Table VI.—PATHOGENESIS OF GANGRENE IN 34 CASES

Extensive main vessel thrombosis	20
Extensive degeneration and thrombosis	5
Extensive small vessel thrombosis	2
Digital thrombosis	4
Peripheral embolism	3

The effect of age on prognosis is directly related to the presence of arteriosclerosis, which will embarrass the development of a collateral circulation. It has been noted in this study that the development of secondary thrombosis in the main vessel after the age of 65–70 years gives rise to immediate gangrene, because of rapidly extending thrombosis (*Table VI*). Such gangrene develops without evidence of prior peripheral arterial insufficiency.

Considering these points, it is of interest to record that gangrene itself carries a varying prognosis, as it may arise in several different ways. Most commonly it is the culmination of many years of peripheral ischæmia with calf claudication, progression to rest pain and skin changes, and finally gangrene. An extensive thrombosis is present and arteriography shows the remains of a collateral circulation (*Fig.* 426). Secondly, gangrene may be the result of digital thrombosis, and except in the case of diabetics, a mere vascular incident. As has been noted, it may come on in old age, when the prognosis is worst. In such cases thrombosis commences possibly at more than one point in an extensively diseased arterial tree,

and extends rapidly. There is virtually no collateral circulation (*Fig.* 427) and gangrene is extensive. Extensive small vessel disease has proved the least common cause of gangrene. Finally, gangrene may result from arterial embolism, the site of impaction in three cases in this series being the popliteal artery. Propagation of the thrombus occurs both proximally and distally, and as there is no collateral circulation (*Fig.* 428), major amputation is required. The incidence of these five types of gangrene in a series of 34 cases is shown in *Table VI*.

SURGICAL CONSIDERATIONS

With the recent advent of direct surgery for the occluded peripheral artery, the recognition of the initial segmental nature of main vessel thrombosis is of great significance, as it makes early diagnosis a necessity if arterial reconstruction is to be undertaken. Delay in diagnosis and treatment will invite the propagation of thrombosis in the main vessel and the development of occlusion in the lower leg arteries. As has been noted, in the early stages the latter are usually free of thrombosis, so that the success of arterial reconstitution in the main vessel will not be compromised.

In the surgical treatment of segmental lower limb main vessel thrombosis by means of an arterial homograft, published series (Hufnagel and Eastcott, 1950, 1951, 1952, Fontaine and Hubinot, 1950, Rob and Eastcott, 1953, Shaw and Wheelock, 1955) have employed an end-to-end anastomosis method, and little attention has been paid to the use of shunt or by-passing vascular grafts. Direct end-to-end anastomoses will lead inevitably to the sacrifice of collateral vessels. As the arteriograms in this series show, the important collateral branches in the area of the adductor magnus opening are especially vulnerable, as one anastomosis will be at this site in about 85 per cent of cases if arterial resection and end-to-end anastomosis with a bridging homograft is contemplated in cases of segmental occlusion. This fact together with the 20 per cent expected early thrombosis rate (Rob and Eastcott, 1953) makes general application of arterial reconstruction by arterial homograft and end-to-end anastomosis probably unjustifiable. A by-pass graft has the great advantage that every collateral vessel is spared. Furthermore, one may select the sites of both proximal and distal anastomoses at the areas of least disease, and arterial resection with its extensive exposure is not required. That such grafts remain patent is apparent from experimental evidence, which also suggests that the incidence of late thrombosis is low (Mavor, 1955). This may be of considerable significance for there is growing clinical experience that the late thrombosis rate in initially patent end-to-end arterial homografts is high and may reach 75 per cent at the end of one year (Linton, 1955).

SUMMARY

1. A study of 149 consecutive cases of atheroma with secondary thrombosis affecting the arteries of the leg is described.

2. The common sites of main vessel thrombosis are indicated, and the usual nature of the collateral circulation in these cases illustrated.

3. Atheroma in the arteries below the knee is discussed in regard to both its clinical manifestations and implications.

4. By the correlation of clinical and arteriographic findings, an endeavour is made to outline the pattern of progression of the disease, and accordingly the prognosis, both in the early stages and with established gangrene.

5. Early diagnosis is essential if treatment by the use of an arterial homograft is contemplated. If the latter is used to produce a shunt or by-pass around the thrombosed segment, considerable advantages result, the most important of which is the preservation of collateral vessels.

I wish to thank Prof. W. C. Wilson for his advice in the study of these patients, who were kindly referred to me by my colleagues. I am indebted to Mr. G. Gordon Bruce for his continued encouragement. My gratitude is also due to Miss Allen of the Radiology Department for her care in the radiographic work, and to Mr. A. Cain of the Anatomy Department for the photography.

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COARCTATION OF THE AORTA ASSOCIATED WITH ANEURYSM

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A REPORT OF THREE CASES TREATED BY AORTIC RESECTION AND GRAFTING

The coexistence of aneurysm and coarctation of the aorta has been recognized with increasing frequency since the introduction of surgery in the treatment of coarctation. Maude Abbott, in her series of 200 cases of coarctation found 14 associated aneurysms, and Gross in 270 cases reported 21 examples, giving an incidence of 7 or 8 per cent. If untreated the majority of the aneurysms rupture sooner or later so that it is a matter of paramount importance to remove the aneurysm or render it inactive. At the same time the coarctation should be excised and the healthy ends of aorta restored to continuity. Exceptionally, this can be achieved by end-to-end suture or by turning down the left subclavian artery into the descending aorta, but more usually the interval between the cut aortic ends requires to be bridged by a homograft.

In this article three cases are described in which the aneurysms and coarctation were excised *en bloc* and continuity successfully restored by an aortic graft. The interest of these cases is that they represent a different pathology in aneurysmal formation—two 'congenital', the third of mycotic origin.

The common site of aneurysm is at the point where a branch (usually an intercostal) comes off the aorta, the swelling tending to spread along this branch. The origin of these aneurysms is obscure though they are similar to those found in the arteries at the base of the brain, and indeed both forms may exist in the same patient. Anatomically the intimal lining is normal and the muscle-fibres in the media normally developed. Muscle apparently plays little part in the tensile strength of a vessel which is largely a function of elastic tissue. The weakness seems to develop in the concentric lamellæ of elastic tissue in the ground substance at a point where the

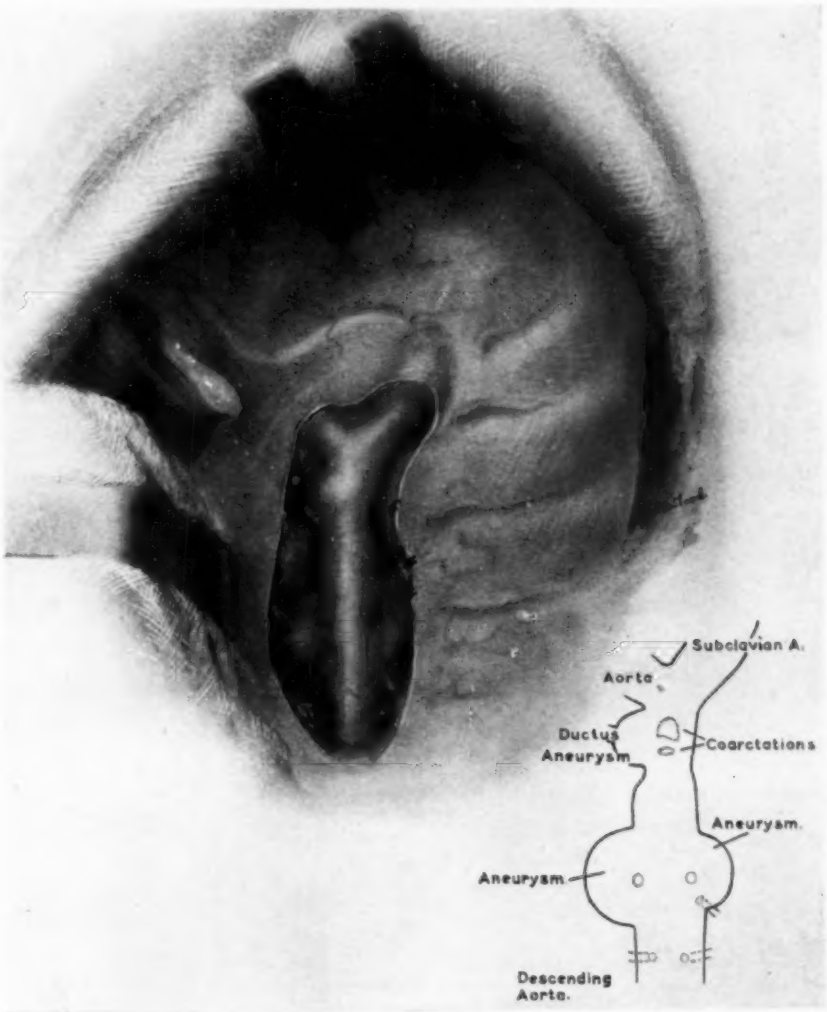

Fig. 429.—*Case* 1. Appearances at operation before resection.

predominantly 'elastic' character of the aorta gives place to its more 'muscular' branch. Most of the aneurysms occur below the coarctation and may be connected with the extreme dilatation of the intercostal arteries.

Bacterial endocarditis is the other cause of aneurysmal formation and the vegetations tend to form just beyond the stricture. The position is somewhat similar to that occurring in persistent ductus arteriosus where the location of the vegetations may be determined by the zone of low pressure or 'slack water' beyond the narrowing. Any weakening of the wall of the artery by infection is an obvious site for aneurysm formation. Maude Abbott's 14 cases of aneurysm were all said to be of mycotic origin.

The presence of an aneurysm may be recognized before operation by straight radiography or following arteriography, but when the dilatations are small they may only be found when the aorta is fully exposed. The aim of surgery should be to resect the coarctation and at the same time to remove the aneurysm. The position is not difficult if the aneurysm and coarctation lie close together as mobilization of the aorta above and below may allow an end-to-end anastomosis without undue tension. If, on the other hand, the aortic stricture is long and the aneurysm is at some distance from the coarctation the use of a graft becomes essential. Before grafts became available treatment of the aneurysm was confined to local excision or minor improvisations which were not as effective as excision.

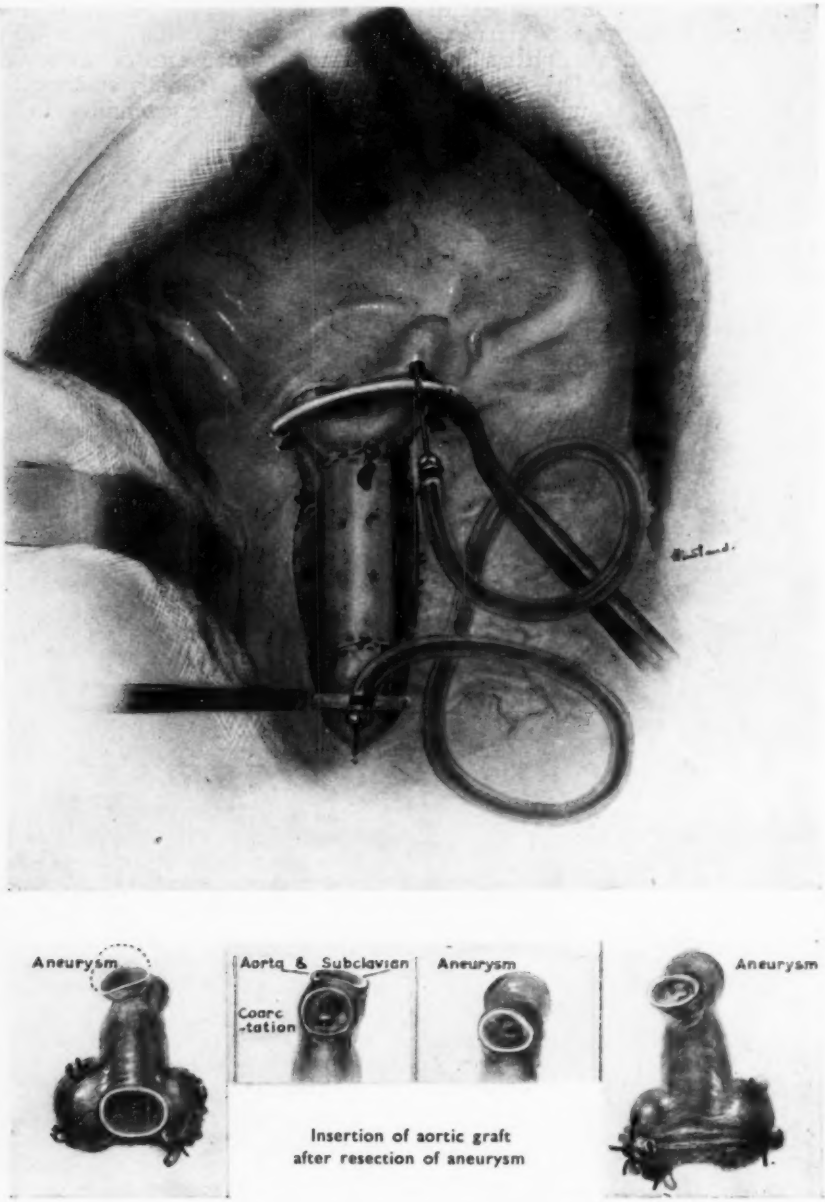

FIG. 430.—*Case* 1. Appearances at operation after resection. The three aneurysms presented close to the coarctation. During insertion of the graft a polythene by-pass tube was used.

CASE REPORTS

Case 1.—D. M., a young woman aged 21 years, was admitted to the Middlesex Hospital under the care of Dr. Somerville with the diagnosis of coarctation. The condition had been diagnosed seven years previously and had been regularly observed since that time.

The patient was well built and active, showing marked arterial pulsation in the neck. The heart was not enlarged and there was an apical systolic murmur. The femoral pulses were weak and delayed. The brachial artery

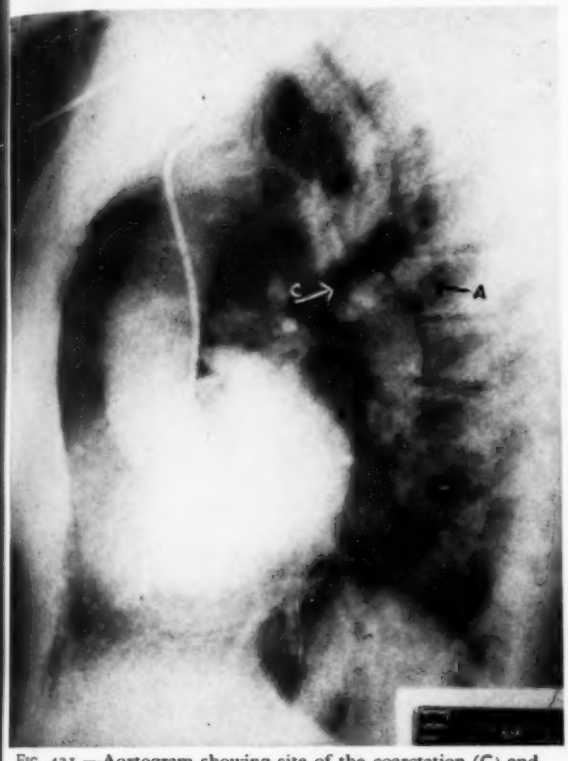

FIG. 431.—Aortogram showing site of the coarctation (C) and just below it the aneurysm (A).

FIG. 433.—Coarctation and aneurysm have been removed showing the opened ends. The loose graft is lying close to the open ends prior to suture.

pressure was 180/115 mm. Hg. Direct interarterial readings gave a brachial pressure of 160/92 and a femoral of 92/54 mm. Hg. There were palpable collateral vessels. Notching of the ribs was visible on radiography and barium swallow suggested that the upper part of the descending aorta was indenting the œsophagus forwards and to the right. The indentation consisted of two areas which were indicative of some dilatations arising from the aorta.

AT OPERATION (Jan. 19, 1955).—A left thoracotomy was performed and the pleural cavity opened after removal of the 5th rib. Hypotensive agents were used with advantage during the actual thoracotomy and early intrathoracic manipulations.

A narrow stricture of the aorta was present just below the greatly dilated subclavian artery and at the same level as the ductus arteriosus. The aortic part of the ductus was swollen up into an aneurysm the size of a large cherry. Below the coarctation two similar sized aneurysms were

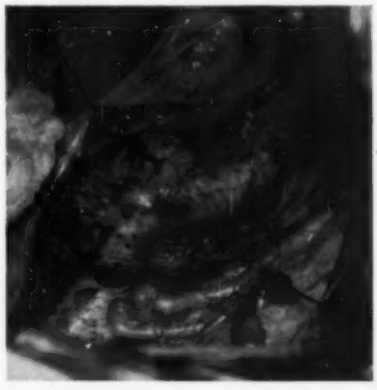

FIG. 432.—Dissection of the aorta showing the coarctation whose external diameter is much greater than the internal opening. Below this lies the aneurysm at the junction of the highest intercostal and descending aorta.

present in the region of the upper right and left intercostal vessels. The walls of these structures were extremely thin and adherent to adjacent tissues. The aortic arch and upper part of the descending aorta were dissected and the aneurysmal area and coarctation freed without undue incident. The pericardium was opened to secure the pulmonary side of the ductus where it existed only as a small channel. Control clamps were applied above and below the aneurysms which were removed *en bloc*, the aneurysm of the ductus being cut across so as to leave a secure stump. (*Fig.* 429.)

An interval 7 to 8 cm. long was left between the divided aortic ends. This was bridged by a homologous aortic graft 8 cm. long and 2 cm. in diameter using an end-to-end junction with each end of the aorta and graft.

FIG. 434.—Specimen showing the thin wall of the descending aorta with the thicker and atheromatous area just above the coarctation.

The graft was prepared by the 'freeze-dry' method and the branches in the graft were closed by sutures before the actual insertion. The junctions were satisfactory and there was practically no loss of blood.

After the central end of the aorta and subclavian artery had been clamped the brachial artery blood-pressure rose from 110 to 160 mm. Hg. A temporary by-pass was provided by inserting two wide bore needles into the aorta above and below the clamps and connecting

them with a silicone-lined polythene tube (*Fig.* 430). The flow through this system caused the blood-pressure to fall to 120 mm. Hg, a figure which was maintained until the end of the operation. The time for the operation was just over 4 hours, during which 2½ pints of blood were given.

Convalescence was completely satisfactory. All pulses in the lower limbs were fully restored. During the first twelve hours after operation the blood-pressure rose to 180/115 but fell to 140/80 by the time that the patient was discharged from hospital 3 weeks later.

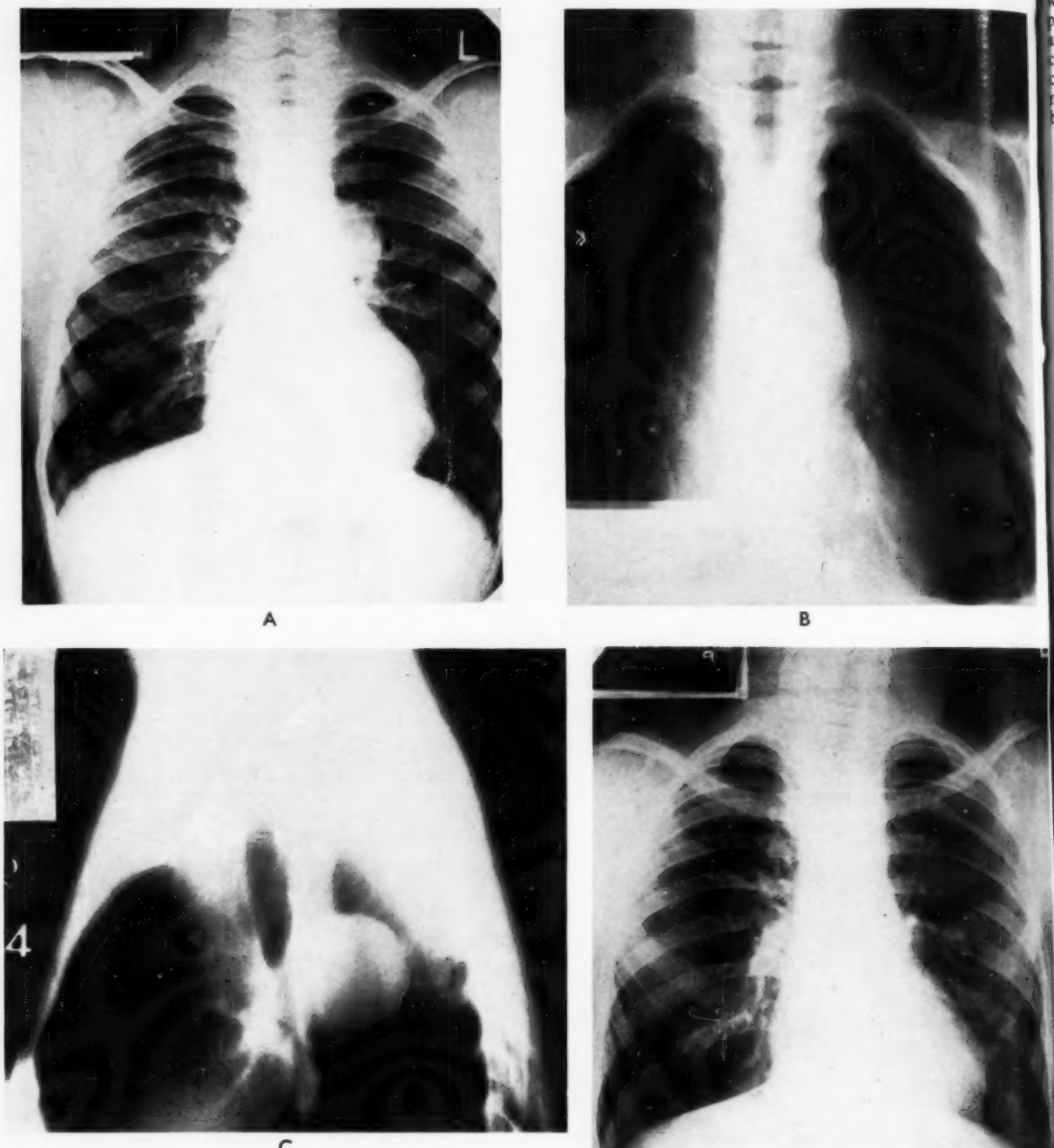

FIG. 435.—*Case* 3. Radiographs. A, Appearance of aneurysm; B, C, P.A. and lateral tomographic views showing the size and site of the aneurysm; D, appearance after operation showing reduction in size of the heart.

The specimen showed a typical coarctation with a internal diameter of 2–3 mm. Just above was the openi into the ductus and below were small orifices, devoid vegetations, leading into each of the two lower aneurysm

Case 2.—D. S., a married woman of 40 years, was admitted to the Middlesex Hospital with the diagnosis of coarctation. She was known to have had heart trouble from childhood, but had suffered little incapacity. At the age of 30, during pregnancy, coarctation was diagnosed, and in the last two or three years she had suffered

from shortness of breath on exertion, and had dizzy spells and palpitations. She also complained of a choking sensation when lying flat.

The patient was a well-built and healthy-looking woman, somewhat flushed and with marked arterial pulsation visible in the neck. The heart was enlarged and there was a systolic murmur heard widely over the chest. Presystolic gallop rhythm was heard. Electrocardiography suggested marked left ventricular enlargement. The blood-pressure was 215/120 mm. Hg in both arms, but no pulses could be felt in any of the leg

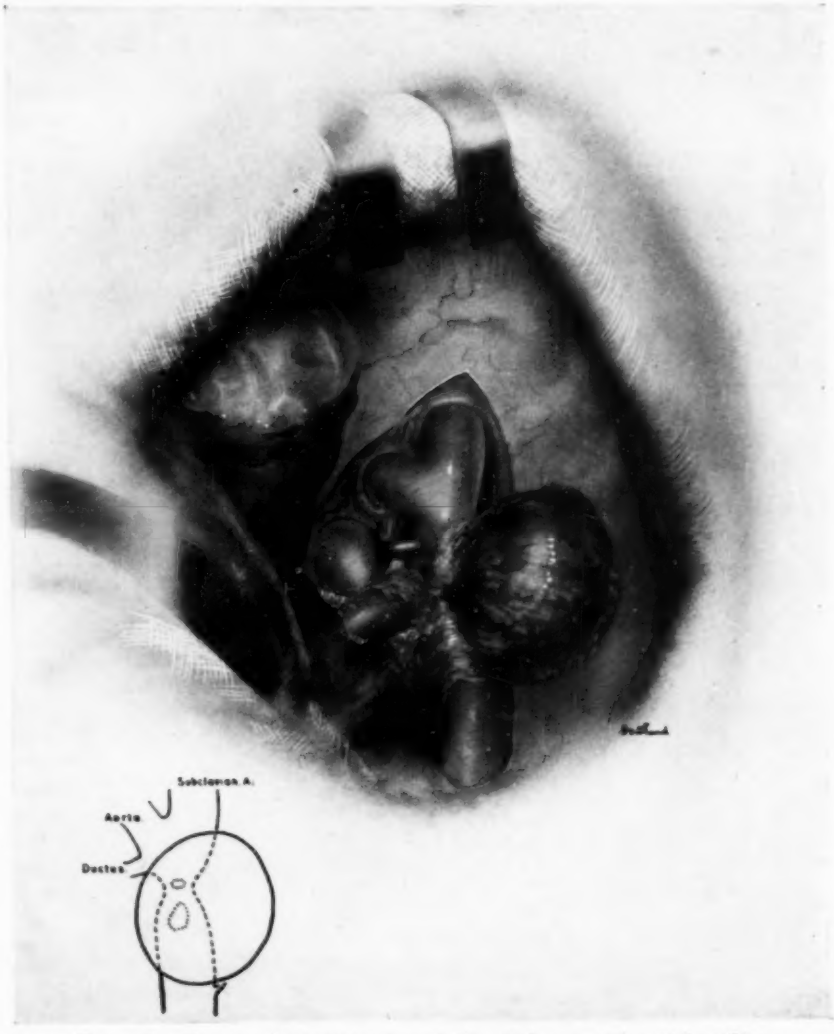

FIG. 436.—*Case* 2. Appearance at operation before resection and grafting.

vessels. A direct pressure reading gave a mean brachial artery pressure of 240, with a diastolic of 150. There were visible and palpable collateral vessels in the front and back of the chest and marked arterial changes in the retinal vessels. Notching of the ribs was present. An angiogram was done by the venous route; this showed a coarctation at the normal site and below this a small aneurysm the size of a cherry (*Fig.* 431).

AT OPERATION (Oct. 15, 1955).—A left thoracotomy was performed and the pleural cavity opened after removal of the fifth rib. Hypotensive agents were used with advantage throughout most of the operation and control of the systolic pressure between 90 and 130 mm. Hg was obtained.

The aortic arch was large and the left subclavian artery of similar dimensions. The coarctation lay at the level of the ductus arteriosus. The descending aorta was of normal size but the highest left intercostal below the coarctation showed a pear-shaped aneurysm with an extremely thin wall. The ductus arteriosus was patent for 3 or 4 mm. away from the aorta (*Fig.* 432).

The whole area above and below the coarctation was dissected free and the upper two intercostals below the coarctation on the left, and one on the right side, were divided. The aorta was clamped above and below the coarctation and aneurysm and the intervening tissue excised, leaving a 6–7-cm. gap. Atheroma was present in the proximal aorta. A 4-cm.-long aortic graft, 2·5 cm. in diameter, prepared by low freezing, was used to bridge the gap. This was sutured to the free ends of the aorta by a single-layer everting type of stitch (*Fig.* 433). The junctions were performed without incident and there was little loss of blood on removal of the clamps. The aorta was occluded for a period of 45 minutes in all. The pleural cavity was drained and the chest closed. Two pints of blood were given during the operation.

At the end of the operation all pulses in the lower limbs were palpable and the condition of the patient was satisfactory. In order to avoid an excessive post-operative rise in the blood-pressure, which has been noted in a number of cases, the patient was given Largactil for four to five days. At the end of a week the patient felt well, the brachial artery blood-pressure was 180/105 mm.

Hg, pulsation in the leg arteries was present, and actually for a short time the patient complained of uncomfortably hot and throbbing feet. She was discharged from hospital 3½ weeks after the operation and her later progress has been satisfactory.

The specimen showed a typical coarctation with an internal diameter of 1 to 2 mm. Above the coarctation was a small dimple at the site of the ductus, and in the lower part was the pear-shaped aneurysm with a very thin wall, opening directly into the aorta by an orifice measuring 6 to 7 mm. (*Fig.* 434).

diastolic murmur suggesting a considerable shunt from aorta to pulmonary artery. The femoral pulses were small and delayed. Blood-pressure in the right arm was 180/100 mm. Hg and in the left arm 160/90 mm. Hg. Angiocardiography was contraindicated owing to iodine sensitivity, but radiographs confirmed the diagnosis of mycotic aneurysm and located it as arising most probably from the descending aorta distal to the site of coarctation. (*Fig.* 435).

AT OPERATION (April 6, 1954).—A left thoracotomy was performed, the chest being entered after resection of

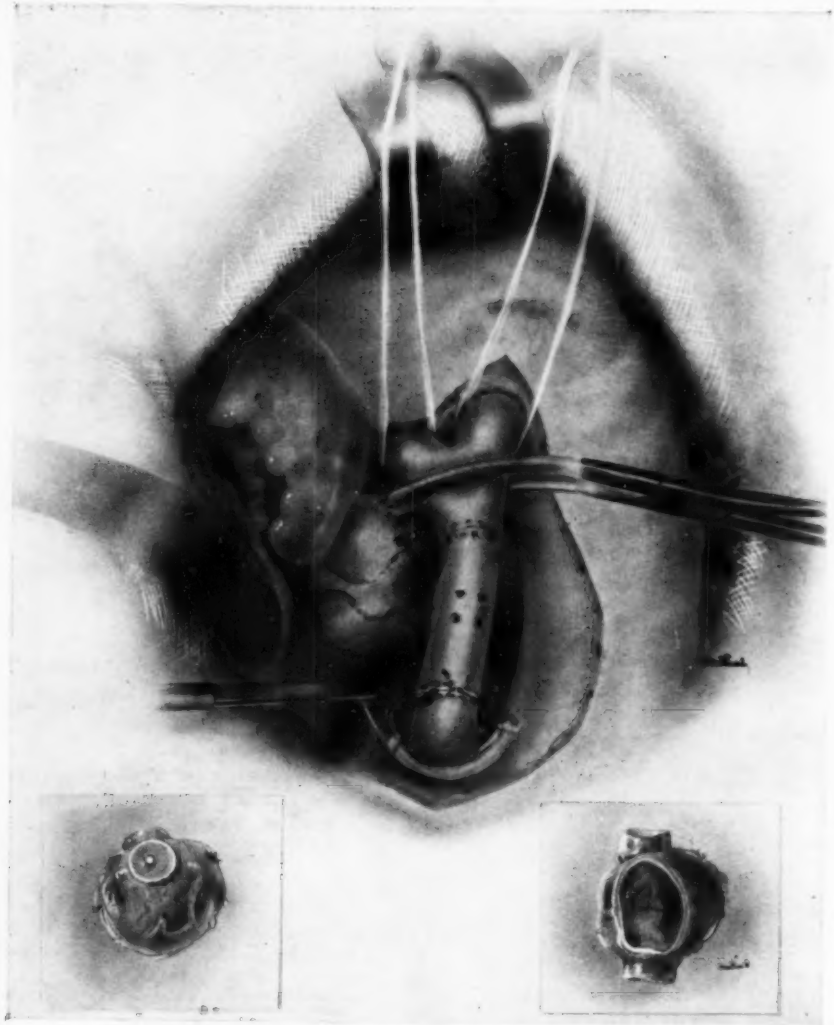

FIG. 437.—*Case* 2. Appearance at operation after resection and grafting.

Case 3. - M. T., a boy aged 9 years, was admitted to the Royal Sussex County Hospital under Dr. Kemball Price in August, 1953, on account of fever and malaise, and signs of coarctation of the aorta and of a patent ductus arteriosus were found. Repeated blood-cultures were positive for *Staphylococcus aureus*, and antibiotic therapy was given altogether for a period of four months before the infection was eradicated. While under treatment a rounded opacity appeared in the left hilar region in the radiograph, and was observed to increase in size. The diagnosis of mycotic aneurysm of the aorta was made and the patient was transferred to the Middlesex Hospital under Dr. Evan Bedford.

On admission, the infection was already under control, and the boy felt well. There was a typical Gibson murmur of patent ductus, and a functional delayed mitral

the 5th rib. It was noted that the vessels in the chest wall were not as large as is usually found in most cases of coarctation.

The condition within the chest was as follows: The aortic arch was small and the left subclavian artery huge, with the coarctation lying immediately below the origin of this vessel. Distal to the coarctation there was an aneurysm at least 2½ in. in diameter and adherent to the adjacent lung and chest wall. The surface of the aneurysm was covered with inflammatory tissue in which the vagus and sympathetic chain were embedded. A small patent ductus appeared to enter the sac, as did several intercostal vessels which were not unduly dilated (*Fig.* 436).

With the aid of hypotensive drugs the blood-pressure was lowered to 90 mm. Hg and the aneurysm and aorta

dissected free. The left vagus below the recurrent laryngeal branch had to be sacrificed and the dissection included a number of enlarged inflammatory glands.

Tapes round the aortic arch, subclavian artery, and descending aorta assisted in the dissection and the ductus and intercostal arteries in the region of the aneurysm were divided between ligatures. A clamp was then placed across the aorta and subclavian above the coarctation and another across the descending aorta well below the aneurysm. The section of aorta containing the coarctation and aneurysm was excised, leaving a deficiency of 6 cm. between the cut ends. This was bridged by an arterial homograft (4·5 cm. long and 1·5 cm. wide) which had been preserved after freezing to — 73° C. After reconstituting the graft, branches arising from it were sutured and two end-to-end anastomoses were performed, using everting sutures of 000 mersylene (*Fig.* 437.) The junctions were satisfactory and the blood-loss was minimal. The aorta had been clamped for just over one hour.

The leg pulses were easily palpable at the end of operation. The pulse-rate was 120, and blood-pressure 150/100 mm. Hg. A temporary water-seal drain was inserted into the pleural cavity.

Convalescence was uneventful though concentration-dilution test suggested mild impairment of renal function for some days post-operatively. The voice was hoarse for a week, but the movement of both vocal cords was normal. The child made satisfactory progress and when seen some months after operation had no symptoms. The blood-pressure in the arms was 140/90 mm. Hg, in the legs 130/80 mm. Hg.

DISCUSSION

In these instances the use of an aortic graft made resection of the diseased area possible. The use of arterial grafts, though originally carried out over forty years ago, has only recently become a practical proposition since the methods of preservation have become more efficient. The grafts used in our patients were prepared by ' deep ' freezing and the ' freeze-dry ' method as described in this country by Rob and Eastcott. The graft affords a scaffolding along which a new intima rapidly grows ; the muscle-fibres degenerate and have probably disappeared within two weeks of implantation, but have been replaced by hyaline connective tissue. The elastic fibres, which are the key to success, show some fragmentation but Creech, DeBakey and their colleagues state that 80 per cent of the fibres exist without fragmentation for at least six months. Aortic grafts have persisted safely in situ for three or four years at least and there has been little evidence of weakening or dilatation of the graft.

The use of a graft for associated coarctation and aneurysm is much less commonly recorded than its use for a long coarctation or aneurysm individually. A graft is not always necessary and Dubost records a case in which the aortic ends could be safely brought together and anastomosed. Alternatively Blalock's manœuvre of turning down the left subclavian artery and joining it to the descending aorta may be considered, but there are some cases in which a graft is essential and one should be available at every operation for coarctation in case its use is necessary.

Considerable attention has been given to the length of time the aorta can be clamped without endangering the peripheral circulation, notably the renal blood-flow. With a normal aortic flow 30–45 minutes is regarded as a safe interval, but in the case of coarctation the flow below the stricture is largely dependent on collateral channels and the time factor of occlusion is not so important. When, however, a graft is used, 45–60 minutes may be required before the double suture line is satisfactorily completed, and in *Case* 1 the use of a ' by-pass ' was clearly of value in preventing the development of too high a central blood-pressure and in providing some additional peripheral flow.

I am indebted to Drs. Kemball Price and Evan Bedford who were in charge of the third case, and to Dr. W. Somerville under whose care the first patient was admitted to hospital. My thanks also go to Miss Hewland who portrayed the operation findings in such an excellent manner.

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OBSTRUCTION OF THE SUPERIOR LONGITUDINAL SINUS BY PLASMOCYTOMA

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MULTIPLE myelomatosis is not a rare disease. The clinical picture, however, in its early stage is vague. There is usually a general disturbance of body function, but the main symptomatology depends upon the site of the myelomatous deposits. Frequently the condition is far advanced before the diagnosis is made, or bone lesions may be discovered in a radiograph taken in the course of routine investigations.

A common feature of myelomatosis is involvement of the bones of the skull and, as a result, disturbance of neurological function may be encountered. In spite of this, however, increase of intracranial pressure would appear to be very uncommon. In a recent review of the neurological features found in this disease Clarke (1954) was able to find in the literature only 7 cases in which raised intracranial pressure had been recorded; he described a further case. A myeloma of the skull may have an intracranial extension, or the tumour may very rarely grow from some intracranial structure. In either case the clinical picture will be common to that of any space-occupying lesion within the skull.

The following case is reported because of the unusual manner of presentation, the increase in intracranial pressure resulting from obstruction of the superior longitudinal sinus.

CASE HISTORY

T. E. T., aged 32 years, was admitted to the Cardiff Royal Infirmary on Jan. 28, 1954. There was a long history of intermittent chronic discharge from the left ear. Nine weeks before admission he had complained of intermittent right pleuritic pain over a period of two weeks. He was then taken ill at work with malaise, shivering, and fever; he was treated at home, recovered in 14 days and returned to work. However, he felt unsteady on his feet, suffered from nausea at times, and vomited. Early in January he developed a stiff feeling in the neck, and occipital headache which was intermittent and occasionally severe, waking him regularly in the early hours of the morning. Two weeks before admission his headaches had become less severe, but he complained of intermittent diplopia and his vision began to fail in both eyes. He was then admitted to hospital.

ON EXAMINATION.—He looked ill and anæmic; there was no pyrexia but his pulse-rate was 110. Blood-pressure was 165/120 mm. Hg. On both sides there was slight proptosis and gross papillœdema with hæmorrhages and exudate. Visual acuity right—J14, visual acuity left—J12. His pupils were dilated but reacted sluggishly to light. Bilateral 6th nerve paresis was present. No nystagmus was detected. Hearing was impaired on the left and examination revealed pus in the external meatus. All tendon reflexes were sluggish; both plantar responses were equivocal, probably flexor. No other abnormal neurological signs were detected.

INVESTIGATIONS.—*Blood*: Red cells, 3,500,000 per c.mm.; Hb., 10·3 g. per 100 ml.; C.I., 1·0; white cells, 7300 per c.mm.; with a normal differential count. *Radiograph of skull*: (*Fig.* 438) There was no evidence of raised intracranial pressure. A rounded translucency, measuring approximately 2 cm. in diameter was noted in the squamous occiput to the left of the midline just above the external occipital protuberance. The margins of the defect were ragged and ill-defined. *Chest radiograph*: Normal. *E.E.G.*: There was no evidence of a focus but a diffuse disturbance was present. *Cerebrospinal fluid*: Pressure, 300 mm.; cells less than 5; protein, 45 mg. per 100 ml.; Lange 1111100000; W.R. negative. *Blood-urea*: 50 mg. per 100 ml. *Urine*: Acid; S.G. 1020; no albumen. *Left carotid angiogram*: No abnormality detected.

PROGRESS.—A provisional diagnosis of toxic hydrocephalus was made and daily therapeutic spinal drainage

FIG. 438.—Radiograph showing the translucency in left squamous occiput.

was carried out. In spite of some reduction in the lumbar C.S.F. pressure there was further loss of visual acuity and slight deterioration in his general condition. Re-examination on Feb. 15 showed that there was now a soft fluctuant swelling, beneath the scalp, superficial to the occipital bone in the region of the translucency demonstrated on the skull radiograph.

In view of the uncertain diagnosis, it was decided to make an exploratory burr hole.

FIRST OPERATION (Feb. 21).—A right frontal burr hole was made. The scalp was indurated and much thicker than normal. All the tissues including the bone were very congested and cyanotic. An attempt was made to carry out ventricular drainage by inserting a polythene tube into the anterior horn. This was not successful as the ventricle appeared to be small, and collapsed after the escape, under pressure, of one or two ml. of C.S.F.

On the morning of Feb. 23 the patient was very drowsy and difficult to rouse. It was decided to explore

the fluctuant swelling in the occipital region as this was now thought to be a tumour, such as a peritorcular meningioma, possibly obstructing the sagittal sinus. At the same time it was proposed to make a subtemporal decompression.

SECOND OPERATION (Feb. 23).—An incision was made over the left occipital swelling and the pericranium divided. Tumour tissue presented through a hole in the occiput, infiltrating the surrounding bone which was definitely thickened. The growth was greyish pink in colour and stringy in consistency. It was continuous with an intracranial mass. It was not possible to determine the full extent of the growth, but the dura was thought to be intact. After a considerable amount of the tumour had been removed the sagittal sinus was exposed on the medial side of the wound, and as far as could be ascertained it was patent. A right subtemporal decompression was made. The dura was quite tense and the underlying brain looked very congested. During these procedures all the tissues had the same congested appearance noted at the previous operation.

The tumour was found on histological examination to be a plasmocytoma. (*Fig.* 439.)

ADDITIONAL INVESTIGATIONS.— *Radiograph of skull* (March 6) : Revealed several small rounded translucencies scattered throughout the vault bones, in addition to the occipital lesion previously noted. Small areas of bone destruction were found in right humerus, left clavicle, left scapula, and right ischium. All these were almost certain myelomatous deposits. *Plasma proteins* : Total protein 8·4 g. per 100 ml. ; plasma fibrinogen 0·4 g. per 100 ml. ; electrophoresis revealed a large amount of an abnormal component in the gamma-globulin region ; electrophoretic serum albumen/globulin ratio, 0·34. *Sternal marrow* : 7·5 per cent of the marrow cells were of plasma variety, some of them appearing atypical and of the myeloma type. *Urine* : No Bence-Jones proteinuria was found on repeated testing.

After the second operation the patient's condition improved steadily. On March 3 he was fully alert, speech function was normal and there were no abnormal neurological signs to be detected in his extremities. The decompression was quite soft and pulsating, and the papilloedema was less. Visual acuity right-finger counting at 9 in., visual acuity left—J14. Lumbar C.S.F. pressure was 250 mm. with normal manometric responses.

Improvement was maintained until March 14 when his condition deteriorated suddenly. He complained of severe headache, and then rapidly passed into coma. His decompression became bulging and tense, and the scalp veins prominent. There was a marked increase in the degree of bilateral proptosis with peri-orbital œdema. Neck rigidity and retraction developed. The right pupil became dilated and fixed to light, while the left remained constricted. The left limbs were very spastic, the right were only slightly hypertonic. Clonus was present in both arms and also at the left knee- and ankle-joints. His plantar responses became extensor. There was some slight response to dehydration treatment but the deterioration in his condition continued and he died the following day without regaining consciousness. Permission for autopsy was unfortunately refused.

DISCUSSION

This patient presented a difficult diagnostic problem and the correct diagnosis was not made until the tumour was examined histologically. There were misleading features in the history, notably the presence of a discharging left ear, the pleuritic pain, and the febrile illness. The common carotid angiogram was normal ; this made an intracranial space-occupying lesion unlikely, although it was not completely excluded. The possibility of a toxic hydrocephalus was considered.

In retrospect not enough attention was given to the small area of bone destruction seen on a radiograph of the skull. The importance of this finding was appreciated only when a fluctuant mass became palpable in relation to this area.

Radiologically, this type of solitary bone defect in vault bones presents no pathognomonic features, and it is seldom possible to make a firm diagnosis without further investigation. The differential diagnosis includes secondary carcinomatous deposit, osteomyelitis, multiple myeloma, syphilitic osteitis, and xanthomatosis ; the latter is an unlikely diagnosis in view of the poorly defined margins of the defect. Rarely, a meningioma may produce changes of this type, (Schinz, 1952) but usually, if it produces any bone changes at all, such a tumour is accompanied by hyperostosis.

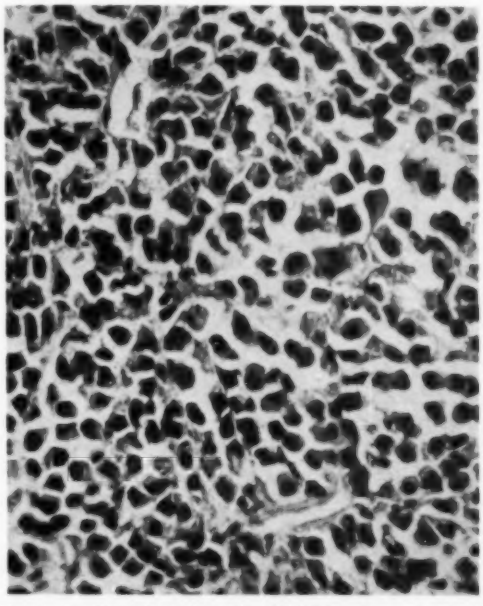

FIG. 439.—Histological section of the tumour. (× 320.)

From the site of the lesion and the clinical picture, obstruction of the superior longitudinal sinus was postulated to account for the increase in intracranial pressure. There seems little doubt that the sinus was obstructed by external pressure, as at both operations the most intense venous congestion of all the tissues including the brain was encountered. The gratifying recovery in a matter of days, after the second operation, was too rapid to be accounted for by the decompression alone. Further, the decompression quickly became soft and the intracranial pressure as judged by lumbar puncture approached normal. It therefore seems most improbable that there was any significant element of thrombosis of the sinus at this stage.

The reason for the patient's deterioration on March 14 was not established for certain, as autopsy was refused. It seems most likely that there was an acute thrombosis of the sagittal sinus in the region of the tumour, as all the signs of marked venous congestion in the head again became evident. Death was thought to be due to medullary failure, the result of a rapid rise in intracranial pressure.

Impairment of the blood-flow in the superior longitudinal sinus may result from primary thrombosis, thrombosis secondary to invasion of the sinus by tumour, and non-thrombotic occlusion from external pressure. Holmes and Sargent (1915) were among the first to stress the importance of sagittal sinus obstruction and to describe the clinical features of the condition.

Parasagittal meningiomata not infrequently produce a slowly progressive obstruction of the lumen of the sinus. Freedman (1953) has emphasized the fact that obliteration of the sinus anterior to the point of entrance of the middle group of cerebral veins is, as a rule, well tolerated, but that rapid occlusion posterior to the Rolandic veins is usually followed by serious disturbance of cerebral function, often fatal. Gradual occlusion, however, as usually occurs in the case of obstruction by a meningioma does not produce such grave consequences. Dandy (1940) pointed out that this was due to the fact that sufficient time elapses for the development of an adequate collateral circulation.

Our case reiterates the seriousness of a rapid occlusion of the superior sagittal sinus. That there was attempted formation of a collateral circulation was evident by the appearance of prominent scalp veins, but this did not prevent the development of increased intracranial pressure. It is interesting to note that in this case, in spite of what must have been an almost complete occlusion of the sinus, there were no epileptic attacks, and there was no evidence of bleeding into the cerebrospinal fluid. Of greater importance however, is the fact that there was no evidence of hemiplegia or paraplegia. This may be explained by the observation of Caudill, French, and Haines (1953) that neurological changes are less likely to occur when the sinus occlusion is by external pressure, than when the obstruction to the blood-flow is of thrombotic origin. As an explanation, it is suggested that, in the latter event, the thrombosis may extend to the cerebral veins, so producing focal cerebral damage. All the symptoms and signs in the case described were due to increased intracranial pressure, the result of venous congestion and cerebral œdema.

SUMMARY

A case of multiple myelomatosis with obstruction of the superior longitudinal sinus is reported. The seriousness of rapid occlusion of this venous sinus posterior to the point of entry of the Rolandic veins is reiterated.

We wish to thank Mr. Charles Langmaid for his permission to publish this case and for his assistance in the preparation of this paper.

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BILATERAL MYCOTIC FEMORAL ANEURYSMS

REPORT OF A CASE WITH SOME REMARKS ON MYCOTIC ANEURYSMS IN GENERAL *

BY LAMBERT ROGERS, CARDIFF

WITH the effective treatment of bacterial endocarditis which has followed the introduction of antibiotics, mycotic aneurysms have become of more interest to surgeons who may be called upon to treat them. At one time of rather academic interest and usually heralding a fatal outcome, these lesions are now complications which, like the disease itself, can be treated with success; resection, endoaneurysmorrhaphy, or Hunterian ligation being carried out according to the site of the aneurysm and the predilection of the surgeon. I have previously recorded examples so treated (Rogers, 1951, 1952) and other reports of the successful surgical treatment of these lesions have come from Harrison and Desmond (1953) and others.

The following is an unusual bilateral case, to which I have not been able to find a parallel. This patient has also responded to antibiotic therapy of the disease and surgical treatment of the aneurysms.

* From the Surgical Unit, Welsh National School of Medicine, Royal Infirmary, Cardiff.

CASE REPORT

Bilateral mycotic aneurysms of the common femoral arteries developing within the course of a few weeks in a young man. Extraperitoneal ligation and division of the external iliac artery on either side.

In the last week of April, 1954, a bricklayer's mate, aged 29, was admitted to a county hospital acutely ill with diarrhœa, vomiting, and pain in the left elbow- and wrist-joints. Numerous petechiæ were present over the body, the temperature was 104° F., he had neck rigidity, and the fluid obtained by lumbar puncture was turbid. There was a systolic murmur at the cardiac apex and he had a history of rheumatic fever in childhood. He developed a swollen and painful left index finger and become doubly incontinent. He was treated with penicillin, sulphatriad, and terramycin, and on May 5 was transferred to the Cardiff Royal Infirmary under the care of my colleague, Dr. Idris Jones. Harsh loud systolic and soft mid-diastolic murmurs were now present and the hæmoglobin was 33 per cent. He was given transfusions of blood and large doses of penicillin and erythromycin. On June 8 a tender, pulsating, expansile swelling appeared in the right thigh below Poupart's ligament. The distal pulses were good. The swelling

continued to enlarge until it was almost the size of a hen's egg and became painful. On June 20 the external iliac artery was exposed extraperitoneally and divided between ligatures. The aneurysm collapsed and did not re-appear. On July 22 a similar pulsating expansile swelling appeared in a corresponding position in the patient's left thigh (*Fig.* 440) and on Aug. 15 the left external iliac artery was exposed extraperitoneally and divided between ligatures. The swelling on this side likewise collapsed and did not re-appear. On Oct. 7 he was discharged, convalescent. He was seen recently, a year after his second operation. He keeps well and is doing light work. (*Fig.* 441.)

FIG. 440.—Seventeen days after extraperitoneal ligation and division of the right external iliac artery of a man aged 29, for an aneurysm which at the time of operation had the same appearance as that now seen on the left side.

FIG. 441.—One year after extraperitoneal ligation and division of the left external iliac artery of the same patient, and slightly more than a year since the same operation was performed on his right side. The scars of both operations can be faintly seen. The aneurysms have disappeared. Circulation in the legs remains adequate and he has no disability.

COMMENT

It is over a century since mycotic aneurysms were first described, L. Koch in 1851 having given an account of one on the superior mesenteric artery which had ruptured in a patient suffering from endocarditis. In 1887 Eppinger, by demonstrating the same organism in the walls of one of them as occurred in the vegetations on the heart valves of the same patient, conclusively proved their pathogenesis. The term 'mycotic' was first used for them in 1885 by William Osler and has now become so well established that it will probably remain, though, as Noble Chamberlain (1943) has pointed out, it would be better to call them 'bacterial' since 'mycotic' has a suggestion of a fungus infection.

In 1923 Stengel and Wolferth collected 217 examples of these aneurysms and as might be expected they were sometimes multiple. In 3 of the patients aneurysms were numerous. They found the aorta was most often involved and next the abdominal vessels (superior mesenteric, hepatic, and splenic). The arms and legs were almost equally involved, the aneurysms occurring chiefly on the brachial and femoral arteries.

It is possible that with early, heavy, and prolonged chemotherapy, complications may occur less frequently in bacterial endocarditis. When aneurysms do appear, however, they are amenable to treatment by proximal ligation, endo-aneurysmorrhaphy, or excision, according to the vessel involved. The patients are usually young, with arteries which elsewhere than at the site of the aneurysm are healthy and there need therefore be no anxiety about the development of an adequate collateral circulation. If the aneurysm is increasing in size or becoming painful delay in surgical treatment may be hazardous.

SUMMARY

A case of bilateral, symmetrically placed, mycotic, femoral aneurysms is described. A Hunterian operation was performed on each side. The aneurysms disappeared and there was no obvious circulatory deficiency.

Now that bacterial endocarditis is amenable to treatment, surgery for mycotic aneurysms is more often required. According to the site of the aneurysm proximal ligation, with division of the artery, endo-aneurysmorrhaphy, or excision may be the procedure of choice.

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RETICULOSARCOMA OF THE THYROID GLAND AND STOMACH

By R. L. CANNEY, Canterbury

CASE REPORT

Mr. B., aged 74, was first seen at the beginning of January, 1952, at the Kent and Canterbury Hospital. He complained of difficulty in swallowing of eight months' duration. This symptom started with a persistent sensation of a desire to swallow. Recently he had not been able to swallow solid food except after very thorough mastication.

A B

FIG. 442.—Anteroposterior radiographs of the neck showing lateral displacement of the trachea and œsophagus. The forward displacement of the trachea is also well demonstrated.

For three months he had noticed attacks of breathlessness, and had noticed that the attacks were worse on lying down but could be relieved by flexing the head. His appetite was good and he had not lost weight. He had no other significant symptoms.

ON EXAMINATION.—His general condition was good for his age. The thyroid gland was considerably enlarged, the left lobe larger than the right, smooth on palpation, and of firm consistency. The whole gland moved freely on swallowing. The trachea was displaced to the right and mild stridor could be produced on full extension of the neck. There were no enlarged lymph-nodes palpable in the neck. There was no evidence of hyper- or hypothyroidism. There were no other abnormal clinical findings.

Investigations.—Straight X rays of the neck and a barium swallow examination were performed. The radiologist's report on the latter was as follows: "The trachea is compressed from side to side and markedly narrowed from behind by a goitre-like mass which displaces it slightly to the right and forwards and compresses and displaces to the right the upper few inches of the œsophagus. There is no evidence of an intrinsic œsophageal lesion". (*Fig.* 442.) The forward displacement of the trachea is well shown in *Fig.* 442 A.

A provisional diagnosis of malignant disease of the thyroid was made and it was decided to perform surgical exploration of the swelling. The diagnosis of lymphadenoid goitre was considered but this was thought to be most unlikely in view of the patient's sex.

AT OPERATION (Jan. 27, 1952).—During intubation before operation, the anæsthetist noted that the left aryepiglottic fold was œdematous but both vocal cords moved normally.

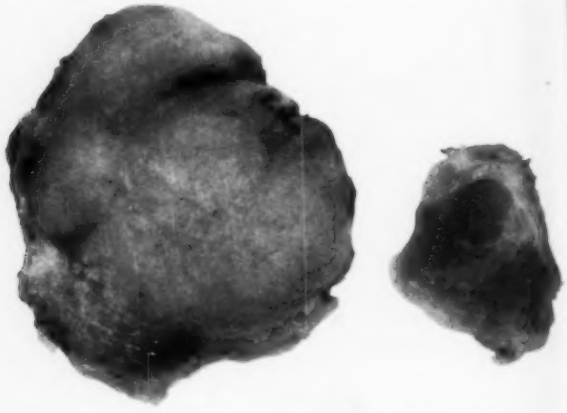

FIG. 443.—Parts of the right and left lobes of the thyroid gland removed at operation. ($\times \frac{2}{3}$.)

The neck was explored through a collar incision. A well-defined enlargement of both lobes and isthmus of the gland was demonstrated, closely adherent to the trachea and extending behind the trachea as a 'collar goitre' and displacing the trachea forwards and to the right. There was no plane of separation between the two lobes of the gland posteriorly. The posterior aspect of the larger left lobe was less clearly defined and appeared to be firmly adherent to the œsophagus in this region. The gland was greyish white in colour.

The whole thyroid gland was removed with some difficulty; the gland was not easy to mobilize, particularly the part lying behind the trachea. The left recurrent laryngeal nerve was seen passing through the tumour and was deliberately sacrificed. During the dissection of the left lobe from the œsophagus, the latter was opened and a tear approximately an inch and a half in length was repaired with two layers of continuous sutures. Two small polythene drains were inserted in the wound.

The patient's immediate convalescence was quite uneventful.

PATHOLOGICAL REPORT.—Dr. J. R. Forbes made the following report on the tumour (*Fig.* 443). The specimen was received in several separate parts, the whole weighing 65 g. The bulk of the specimen consisted of white homogeneous neoplastic tissue which had replaced all the thyroid gland except the upper pole and the extreme periphery of the left lateral lobe. The neoplasm in this lobe was discoid in shape and slightly lobulated, and measured 5 × 2 × 2 cm. It was quite well defined but at several points infiltrated the residual thyroid tissue, which was compressed and rather tough. The tumour itself was of brain-like consistency and the gross appearance was that of sarcoma.

Microscopical examination revealed a highly cellular neoplasm composed of closely packed pleomorphic cells, predominantly of reticulum-cell type (*Figs.* 444, 445). These had large vesicular nuclei measuring 10-20 μ in diameter, with prominent nucleoli and a network of

chromatin threads and granules. Cytoplasm was scanty or absent and stained feebly with eosin. Mature lymphocytes were plentiful and were seen in clump and singly. Eosinophil polymorphs were scattered throughout the tumour in moderate numbers. Sections stained

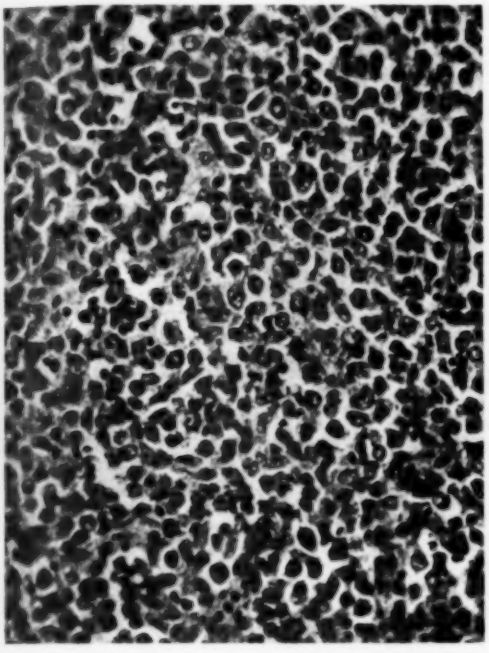

FIG. 444.—Photomicrograph of thyroid tumour. (×275.)

selectively showed an interlacing network of fine reticulin strands mainly around clumps of reticulum cells, but also around individual cells.

The peripheral parts of the tumour had infiltrated the adjacent thyroid tissue and invaded small blood-vessels; in part, the growth had penetrated the capsule with invasion of skeletal muscle.

The histological picture is consistent with reticulum-cell sarcoma of the thyroid, but with features suggestive of atypical Hodgkin's disease (*Fig.* 446).

PROGRESS.—In view of the above report, the patient was referred to Dr. A. D. O'Connor, Consultant Radiotherapist at the Kent and Canterbury Hospital, who agreed to commence a course of post-operative radiotherapy. Treatment was started on the fourteenth post-operative day. He had a maximum dose of 4000 r, minimum dose of 3000 r, in eighteen days at 200 kv.

The patient had a very severe reaction to the treatment, with marked tracheitis and pharyngitis. This improved with treatment with inhalations and an expectorant mixture.

He was discharged from hospital reasonably comfortable on a maintenance dose of thyroid extract. He was seen at regular intervals as an out-patient; his general condition remained satisfactory except on one occasion he appeared definitely myxœdematous and his dosage of thyroid extract was considerably increased. Ten months following operation his voice was weak and hoarse; there was no evidence of recurrence in the neck but some induration in the left posterior triangle.

SUBSEQUENT HISTORY.—The patient was sent by his doctor to the Out-patient Department at the Margate General Hospital in December, 1953, eleven months following his operation for total thyroidectomy. He stated that he felt well and his neck was now causing him no trouble but he complained bitterly of abdominal pain of several weeks' duration. The pain was not related to meals, nor had he found any means of relieving his discomfort. He complained of persistent nausea and retching but had not vomited. His appetite was fair and he stated that he had not lost weight. His bowels were constipated and he had noticed black motions on two occasions.

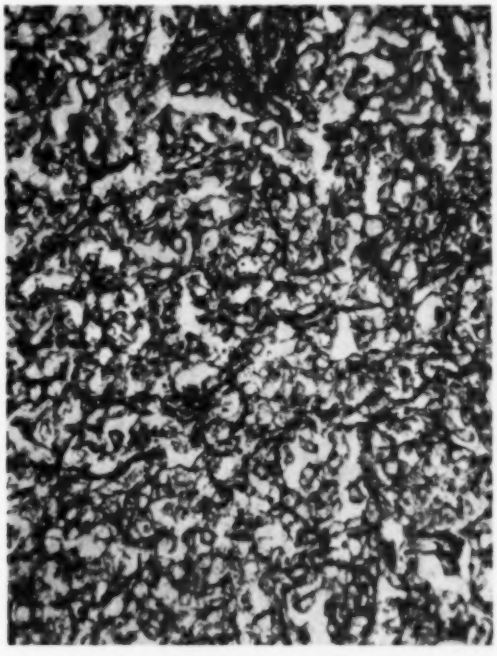

FIG. 445.—Photomicrograph of thyroid tumour with reticulin stain. (×275.)

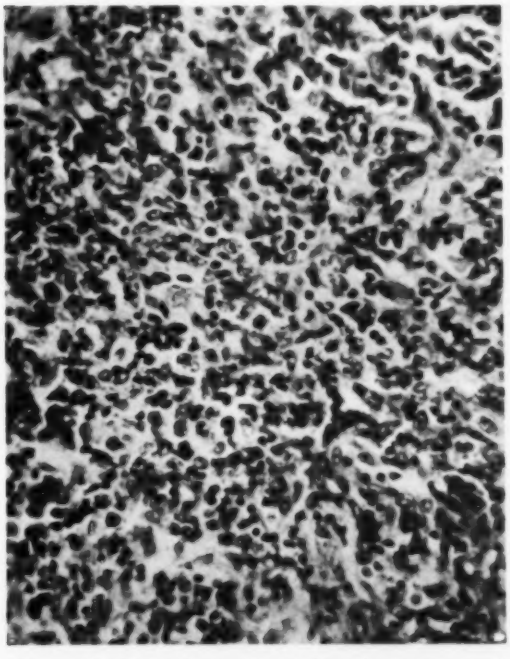

FIG. 446.—Photomicrograph of thyroid tumour showing resemblance to Hodgkin's disease in part of the tumour. (×240.)

Examination.—His general condition was fair. There was still no evidence of a recurrence in the neck. There was no abnormality found on abdominal or rectal examinations.

Investigations.—Hæmoglobin 81 per cent. Blood-urea 50 mg. per cent. Radiograph of chest showed normal appearance. A barium meal radiograph showed a large crater on the greater curvature of the stomach with a deep central niche (*Fig.* 447).

FIG. 447.—Radiograph of stomach showing large ulcerated lesion on the greater curvature.

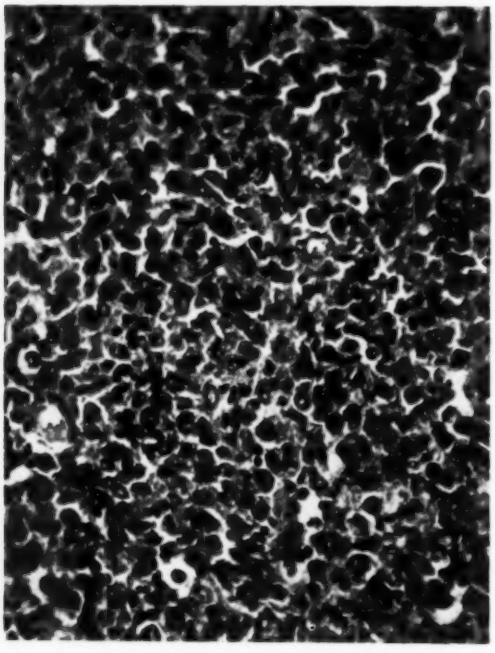

FIG. 449.—Photomicrograph of tumour from stomach. (× 275.)

A provisional diagnosis of carcinoma of the stomach was made and laparotomy was advised. The patient was very unwilling to undergo further ordeal by surgery but after some persuasion agreed to come in to hospital.

AT OPERATION (Jan. 6, 1954).—Laparotomy was performed in the Margate General Hospital after routine pre-operative preparation. The abdomen was opened through an upper left paramedian incision. A large ulcer approximately 2 in. in diameter was palpable high on the greater curvature of the stomach; the surface of the stomach appeared normal. The liver was normal in appearance and on palpation. There were a few enlarged soft lymph-nodes present along the greater curvature of the stomach. There were no other abnormal findings.

FIG. 448.—Part of the stomach removed at operation. Unfortunately a large part of the normal stomach has been trimmed away for the purpose of mounting. (× ½.)

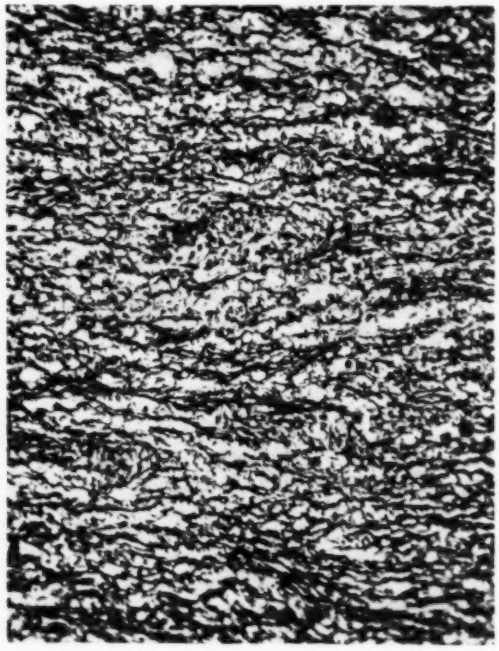

FIG. 450.—Photomicrograph of tumour from stomach. Reticulin stain. (× 120.)

A high subtotal gastric resection was performed with approximately 2 in. of normal stomach wall proximal to the ulcer edge.

PATHOLOGICAL REPORT.—Dr. H. Sterndale made the following report on the specimen. The specimen consisted of most of the stomach including the pylorus. It measured 10 cm. along the lesser curve and 15 cm. along the greater curve. There was a large ulcer of the greater curvature at the fundal end of the stomach. The ulcer was circular, measuring 4 cm. in diameter, with a raised, rolled, and undermining edge. The crater was up to 1 cm. in depth and the floor was smooth and showed tiny punctate hæmorrhages (*Fig.* 448).

Microscopical examination of the ulcer showed a very cellular tumour of predominantly reticulum-cell type, having the same characteristics as the cells of the thyroid tumour. It was a reticulosarcoma (*Figs.* 449, 450).

The sections of this and the thyroid tumour were seen by Dr. J. W. Whittick, of the Royal Cancer Hospital, who confirmed the diagnosis of reticulosarcoma.

PROGRESS.—The patient's convalescence was uneventful but slow, and he was discharged from hospital three weeks after operation. He has been seen regularly at three-monthly intervals, remains well, and has no clinical evidence of recurrences. His myxœdema is well controlled by thyroxin and at the time of writing four years have elapsed since he was first seen.

DISCUSSION

Cases of reticulosarcoma of the thyroid gland are undoubtedly uncommon. An unusual feature of these tumours is a tendency for foci of similar tumours to occur in other sites, notably the gastro-intestinal tract.

Aird (1949) states that a sarcoma arising in the thyroid is an excessively rare tumour. Dick and Kellett (1951), in this JOURNAL, report two cases with metastases in the gastro-intestinal tract found at autopsy. Kellett and Sutherland (1949) report 5 cases and refer to 10 other cases in the surgical literature. Scott (1952) reports 2 cases and Brewer and Orr (1953), in a very comprehensive paper, describe 10 cases and review 13 other collected cases. In 2 of their cases metastatic deposits were found in the wall of the intestine. In their collected cases, 3 only had post-mortem examination performed, all of which had metastases in the alimentary tract.

The main interest in these tumours centres around the question whether they are in fact truly neoplastic. No case has been reported with metastases in the lungs, though lymph-node involvement occurs. The distribution of the metastases in reported cases is certainly most unusual and involves a very high incidence of gastro-intestinal deposits arising after the removal of the thyroid tumour. Some writers have even suggested that the condition may be a granulomatous one, with a predilection for the thyroid and the wall of the gastro-intestinal tract.

Kellett and Sutherland also discuss in some detail the possible relationship of the condition with struma lymphomatosa, but can find no evidence that the latter is a precursor of reticulosarcoma. If, in fact, the condition is a true tumour, there is also doubt whether the metastases that occur are lymphatic or blood borne.

The pathology of the tumour is extremely complex. There has always been difficulty in differentiating sarcoma and carcinoma of the thyroid histologically, and some have even doubted whether sarcoma occurs at all in the thyroid gland. The exact nature of the tumour is often not certain following microscopical examination.

Collateral evidence, such as the discovery of a similar tumour in another site, is often the only positive confirmation of the diagnosis and this was certainly so in the present case, when the diagnosis was only confirmed absolutely following the removal of the second tumour. It seems doubtful whether the diagnosis can ever confidently be made without such collateral evidence.

Reference to previously reported cases appears to show that when the secondary tumours occur in other sites, the small intestine is the most usual situation, though metastases have been discovered in the retroperitoneal and retrosternal tissues and in the para-aortic lymph-nodes. Scott reports a case with a secondary tumour in the kidney and a case with two secondary lesions in the stomach, the latter discovered at autopsy. The gross appearance of the gastric lesions was very similar to that of the present case.

I can find no record of a case in which both thyroid and abdominal tumours have been removed surgically, all previous cases of intra-abdominal metastases having been post-mortem findings.

Obviously if a diagnosis of reticulosarcoma is suspected following removal of a thyroid tumour, careful investigation of the gastro-intestinal tract should be undertaken.

All writers on this subject agree that these tumours rarely occur before the age of 60 and most commonly in females. All 5 cases in Kellett and Sutherland's series were in elderly women. One case of the 13 cases reported by Brewer and Orr was a male and all cases were 60 or over. The case now reported is thus unusual, the tumour being found in an elderly male.

These tumours appear to be radio-sensitive and most cases treated surgically have had supplementary radiotherapy.

SUMMARY

A case of reticulosarcoma of the thyroid gland treated by total thyroidectomy and radiotherapy is reported. An associated reticulosarcoma of the stomach was removed surgically at a later date.

The case report is followed by a short survey of the literature of the condition.

My thanks are due to Dr. H. Sterndale, of the Margate General Hospital, and Dr. J. R. Forbes, of the Kent and Canterbury Hospital, for the pathological reports and their help in the preparation of this paper.

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ROUND-CELL TUMOURS OF BONE

By GEORGE LUMB and D. H. MACKENZIE
WESTMINSTER HOSPITAL, LONDON

The use of the biopsy in the diagnosis of lesions of bone has long been a source of controversy, and it is of paramount importance that the information provided by the examination should be so reliable that it becomes an essential part of the investigation of the patient. Once it is established that a malignant tumour is present in a bone, it is then placed in one of two categories depending on whether its cells are predominantly round or spindle-shaped.

When a uniformly round-cell tumour is found it may be a metastatic deposit, and those originating from a primary neuroblastoma present special problems. It may be a primary tumour arising from hæmopoietic bone-marrow, or a round-cell primary tumour of uncertain origin. This latter group includes those cases which have been described as Ewing's tumour, the exact origin of which is still in dispute. It also includes the so-called primary reticulum-cell sarcoma of bone, although some authors, such as Stout (1943), have suggested that no true differentiation can be established between this tumour and Ewing's tumour. The differentiation of tumours derived from hæmopoietic marrow usually presents no great difficulty, for their cells are of characteristic appearance (Lumb and Prossor, 1948; Geschickter and Copeland, 1949; Lumb, 1952). The problem of distinguishing metastatic carcinoma, neuroblastoma, Ewing's tumour, and reticulum-cell sarcoma presents much greater difficulty. It must be remembered that even in young people (Hirsch and Ryerson, 1928) metastatic deposits in bone from carcinoma of the bronchus may be the presenting feature of this disease. However, it is the differentiation between Ewing's tumour, primary reticulum-cell sarcoma of bone, and metastatic neuroblastoma in bone which presents the greatest difficulty. With this in mind it was decided to extract from the records of Westminster Hospital during the past twenty years those cases where the presenting feature was a bone tumour in which round cells predominated and myelomas and metastases other than those from a neuroblastoma could be excluded. Twenty-three cases in which adequate information was available are reviewed. Before these are presented a general summary of the three tumours under discussion will be given.

1. Ewing's Tumour.—In 1921 James Ewing described bone tumours "which differed markedly from osteogenic sarcoma, were not identical with any known form of myeloma, and which had to be designated by the vague term round-cell sarcoma of unknown origin and nature".

Based on this experience he proposed that there existed "a rather common tumour occurring in young subjects, commonly identified with osteogenic sarcoma and usually called round-cell sarcoma, which is really of endothelial origin, and which is marked by such peculiar gross, anatomical, clinical, and therapeutic features as to constitute a specific neoplastic disease of bone". The characteristics of this condition as defined by Ewing were :—

a. It occurs in young people—all Ewing's original 7 cases were between 14 and 19 years.

b. The tumours are rather slow growing, diffuse, and soft, and may invade surrounding soft tissues. The ends of the bones are spared, in sharp contrast with osteogenic sarcoma and osteoclastoma.

c. Pain, tenderness, and fluctuation in size are frequent.

d. Pyrexial attacks may occur.

e. Response to initial treatment by irradiation is immediate and striking.

f. Radiographs have characteristic features on which a diagnosis can be based with considerable confidence.

g. Histological examination reveals sheets of small polyhedral cells with pale cytoplasm, small hyperchromatic nuclei, well-defined cell borders, and complete absence of intercellular material.

In the following years a large number of cases of Ewing's tumour were described in the American literature by such authors as Connor (1926) and Copeland and Geschickter (1930). They accepted Ewing's statements regarding the specificity of the clinical and radiological picture, but autopsy reports were rare. A more recent contribution is that of McCormack, Dockerty and Ghormley (1952). The exact origin of the tumour has long been in dispute. Ewing (1921) himself, and later De Santo (1934), and Foot and Anderson (1941), considered that it arose from endothelium. Oberling (1928), Oberling and Raileanu (1932), Melnick (1933), and Lichtenstein and Jaffe (1947) suggest an origin from primitive mesenchymal cells, whilst Geschickter and Copeland (1949) thought that the origin might be from a lymphoblast, and Roome and Delaney (1932) from a myeloid stem cell or hæmocytoblast.

2. Primary Reticulum-cell Sarcoma.—It was Oberling (1928) who first suggested that a primary differentiated reticulosarcoma of bone existed, and Ewing himself accepted it as an entity in 1939. In that year Parker and Jackson described 17 cases, while Edwards (1940) described a case which came to autopsy. Two further accounts are those of Coley, Higinbotham, and Groesbeck (1950), who described 37 cases, and McCormack, Ivins, Dahlin, and Johnson (1952), with 25 typical cases.

Reticulum-cell sarcoma of bone usually occurs later in life than Ewing's tumour. The cases of Coley and others (1950) averaged 33·7 years, and those of McCormack and others ranged from 11 to 66 years, with an average of 37. In the cases described by Parker and Jackson 77 per cent were below the age of 40 and 30 per cent below 20 years of age. It occurs more commonly in men than women, and in the series of McCormack and others 19 were male and 6 were female. It is usually situated in one of the bones of the extremities. The main presenting symptom is pain accompanied by varying degrees of disability. In many cases the patient complains of

a lump which can usually be palpated. In the series of McCormack and others 76 per cent of patients gave a history of twelve months or less. The tumours tend to be large, soft, friable, and glistening. They are greyish-pink to white in colour, with areas of necrosis. Erosion of cortex and marrow is a common finding. X-ray appearances are not pathognomonic, though Sherman and Snyder (1947) suggest that the diagnosis can be suspected on radiological grounds alone. The blood-chemistry is usually within normal limits. These tumours are very radio-sensitive. Histologically the appearances are variable but the essential component is the reticulum cell. This is two to four times the size of a lymphocyte, has abundant pale-staining cytoplasm, and a well-defined nucleus and nucleoli and an easily recognizable chromatin network. Binucleated cells may occur, but true Sternberg-Reed cells are not seen. The stroma is loose and vascular. Reticulin fibres may encase individual cells or may surround small groups. Valls, Muscolo, and Schajowicz (1952) claim that the distribution of reticulin is quite different from that observed in Ewing's tumour. Cells closely resembling lymphocytes may also be present.

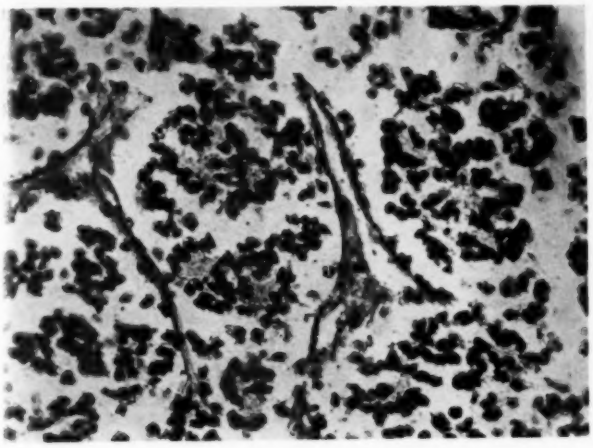

FIG. 451.—*Case* 2. A neuroblastoma showing absence of reticulin. Silver impregnation. (× 65.)

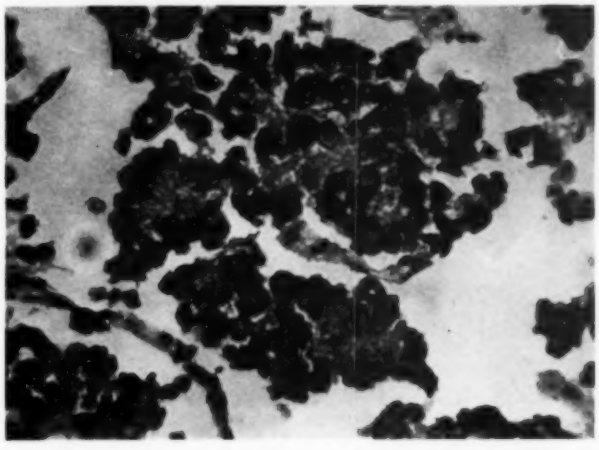

FIG. 452.—*Case* 2. A neuroblastoma showing high-power view of typical rosettes. Hæmatoxylin and eosin. (× 195.)

Schajowicz and Cabrini (1954) state that periodic acid Schiff-positive granules can be demonstrated in the cellular cytoplasm in cases of Ewing's tumour, whereas they are not observed in reticulum-cell sarcoma. In our series all the cases of reticulum-cell sarcoma gave negative results, but no very convincing positive reactions have been observed. Two cases of Ewing's tumour and one neuroblastoma showed occasional P.A.S.-positive granules.

3. Neuroblastoma.—A neuroblastoma is a malignant tumour, usually occurring in children. It arises either from the undifferentiated proliferating neural tissue of developing sympathetic ganglia or from the adrenal medulla, and it cannot be emphasized too strongly that it may arise from any part of the sympathetic system. As Willis (1953) points out, there is general agreement that fully differentiated nerve-cells are incapable of multiplication. Neuroblastomas and the more differentiated ganglioneuromas must therefore arise before full maturity of the nerve-cells is reached, and it is not surprising that transitional and mixed forms occur (Dunn, 1915; Wahl and Craig, 1938; and Willis, 1953). It is also possible for neuroblastomas to mature and acquire the benign nature of the ganglioneuroma (Cushing and Wolbach, 1927; Wells, 1940; Eden, 1941; Wyatt and Farber, 1941). This fact is clearly of the utmost importance in cases of apparent Ewing's tumour with a long survival time. Here the possibility arises that the bone lesion may be a secondary neuroblastoma in which the primary growth became differentiated after metastasis to the bone had occurred.

The first cases which can be accepted as being definite neuroblastomas were described by Abercrombie (1880) and separately by Parker in the same year. They were called sarcomas. Later workers, such as Küster (1905) and Schilder (1909), regarded similar tumours as being gliomas, an opinion which was short-lived. The fact that the histology of these tumours resembled that of the developing sympathetic ganglia was finally established in the important paper by Wright (1910). There have been many subsequent communications, notably those of Herxheimer (1914), who demonstrated that the fibrils in an adrenal neuroblastoma were fine nerve-fibres; Landau (1912) and Wahl (1914), who drew attention to the range of structural differentiation in this group of tumours; Robertson (1915), Wahl and Craig (1938), and Blacklock (1934), who showed that combinations of neuroblastomas and differentiated ganglioneuromas could occur; and Rix and Geschickter (1938), Willis (1953), and others, who recorded the extremely important observation that neuroblastomas may occur in adults.

In many, but not all cases the cells group themselves in rosette-like clusters within which neurofibrils can be seen. It should be stressed, however, particularly in biopsy material, that rosettes may be absent. For this reason the diagnosis of neuroblastoma is often one of great difficulty when the first clinical manifestation is a solitary bone metastasis. Convincing rosette formation was only observed in bone in one of the five proven cases of neuroblastoma in this series, whereas it was frequently encountered in the soft-tissue metastases. In addition it is possible that cell size may be influenced by

environment. Thus in *Case* 16 the bone tumour showed small cells with very darkly staining nuclei, whereas in the lymph-node metastases the cells were larger and the nuclei were more palely staining. As will be seen later in this discussion, the question of cell size and appearance is a feature of fundamental importance when an attempt is made to distinguish reticulum cells from those occurring in Ewing's tumour.

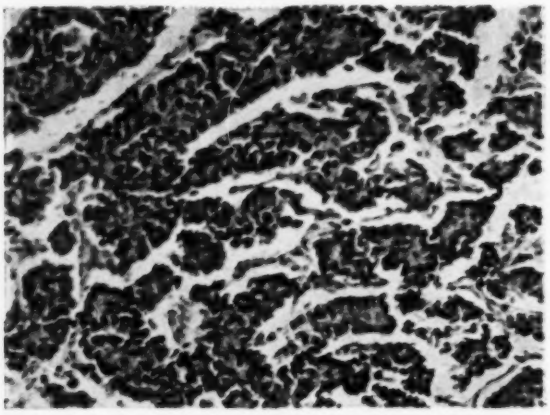

FIG. 453.—*Case* 2. A neuroblastoma showing numerous rosettes. Hæmatoxylin and eosin. (× 86·5.)

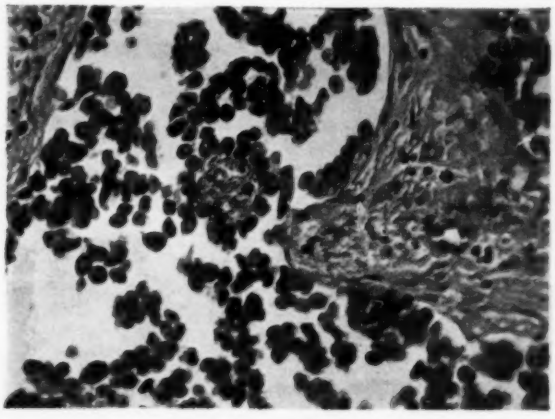

FIG. 454.—*Case* 5. A neuroblastoma showing a pseudo-rosette with necrotic cells in the centre. Hæmatoxylin and eosin. (× 200.)

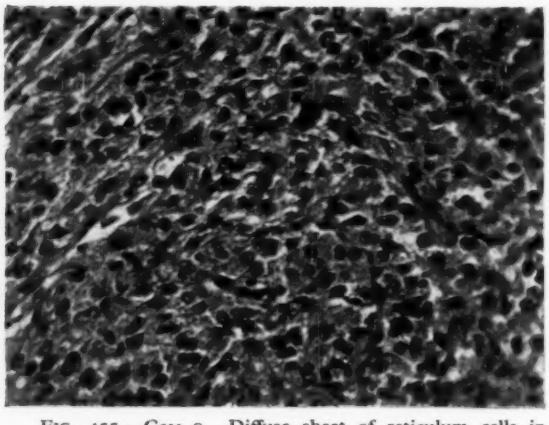

FIG. 455.—*Case* 9. Diffuse sheet of reticulum cells in reticulum-cell sarcoma of bone. Hæmatoxylin and eosin. (× 233.)

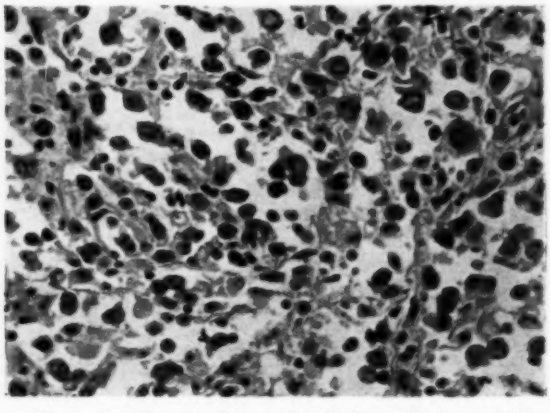

FIG. 456.—*Case* 6. Scattered reticulum cells in reticulum-cell sarcoma of bone. Hæmatoxylin and eosin. (× 233.)

With these considerations in mind the histological appearances of the twenty-three cases under discussion have been placed in the following groups :—

Group I. Five Cases of Neuroblastoma.—In 4 of these autopsy revealed primary tumours of the sympathetic nervous system. In the remaining example the histological appearances were unequivocal in that classical rosettes were seen in large numbers.

The neuroblastoma arises from pluripotential cells of the sympathetic nervous system and typical tumours are composed of aggregates of cells, usually spheroidal in shape, but sometimes pyriform in outline. They are darkly staining and nuclear chromatin is usually closely aggregated. Nucleoli are uncommon. Cytoplasm is minimal and silver impregnation shows very scanty reticulin (*Fig.* 451). The most characteristic histological feature is the tendency for the cells to arrange themselves in rosette-like clusters, with a central eosinophilic area in which neurofibrils can sometimes be demonstrated (*Figs.* 452, 453). In other areas the direction in which the sections are cut may show longitudinally arranged neurofibrils. It has been emphasized already that rosettes are not a constant feature of this disease process, and it will be realized that the cell itself has no specific character in the absence of neurofibrils. Furthermore, the grouping of cells around small blood-vessels or the necrosis which may occur centrally in a closely packed cellular clump may give a pseudo-rosette appearance (*Fig.* 454). Careful examination, however, will always reveal either the small central blood-vessels or the ghosts of necrotic cells.

Group 2. Four Cases of Reticulum-cell Sarcoma.—In 2 of these an autopsy revealed generalized reticulum-cell sarcoma of lymphoid tissue. In the third case, in which the primary growth was in the femur, the disease involved the inguinal glands, whilst in the fourth the lesion has remained localized. The histological picture consisted of a replacement of normal architecture by sheets of large cells varying from 12 to 20 μ in diameter, with large, well-defined nuclei frequently containing one or more weakly eosinophilic nucleoli (*Figs.* 455, 456). The cytoplasm was irregular in quantity and outline and stained palely with eosin. An important problem in differential diagnosis is to distinguish reticulum-cell sarcoma from metastatic anaplastic carcinoma. In

the former, silver-impregnated sections show reticulum fibres scattered diffusely among the cells, and sometimes interlacing prolongations join one cell with its neighbour (*Fig.* 457), whereas in carcinoma the reticulin framework usually surrounds clumps of cells.

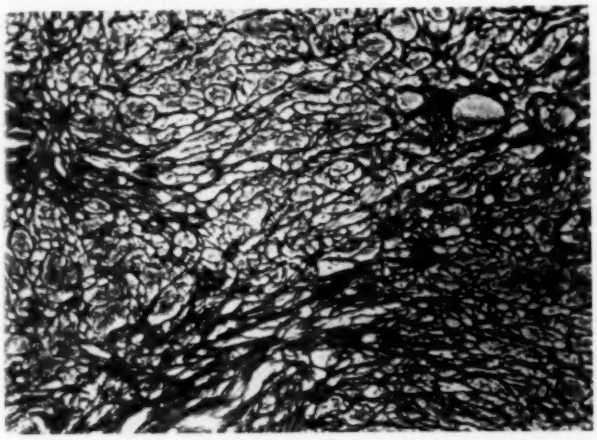

FIG. 457.—*Case* 9. Dense reticulin network in reticulum-cell sarcoma of bone. Silver impregnation. (× 150.)

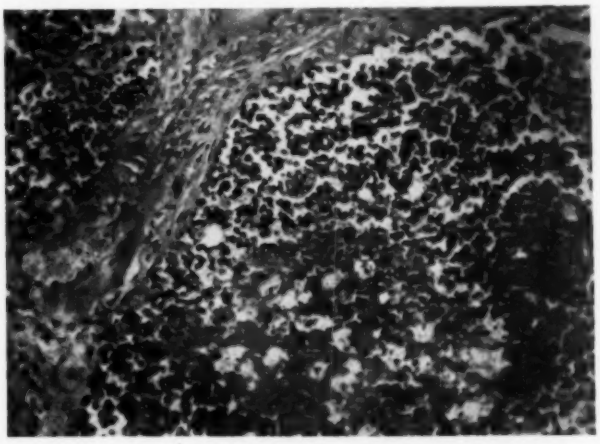

FIG. 458.—*Case* 10. A Ewing's tumour showing the characteristic sheets of round cells. Hæmatoxylin and eosin. (× 110.)

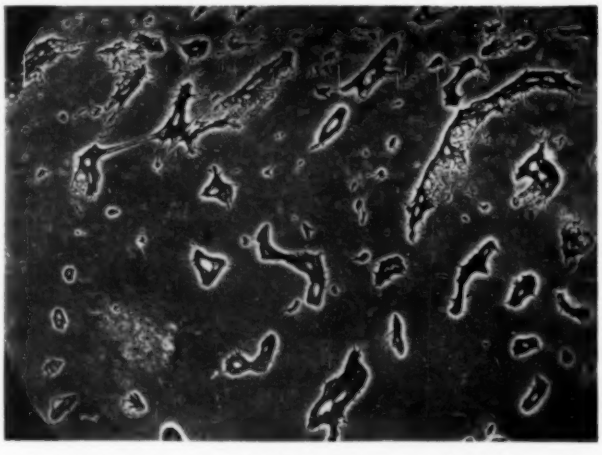

FIG. 459.—*Case* 16. A Ewing's tumour showing absence of reticulin network. Silver impregnation. (× 50.)

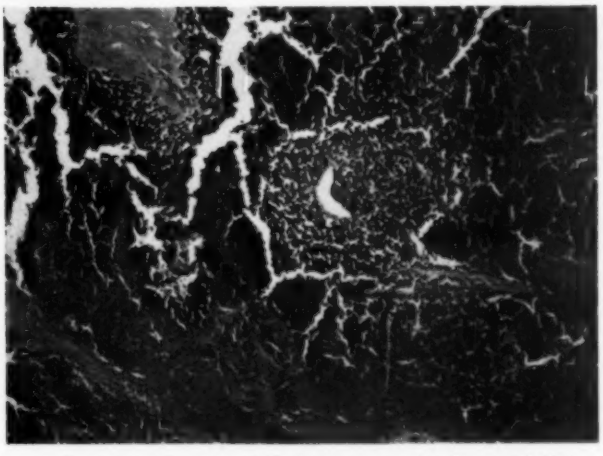

FIG. 460.—*Case* 15. A Ewing's tumour showing perithelial cellular arrangement and extensive necrosis. Hæmatoxylin and eosin. (× 65.)

commonly found in these tumours, and the irregular distribution of surviving cells around small vessels constantly produced a perithelial arrangement (*Figs.* 460, 461). Special attention should be drawn to the autopsy findings in *Cases* 17 and 19, where multiple small tumours were found in both suprarenals in *Case* 17 (*Fig.* 462) and in one suprarenal in *Case* 19. These were situated in the cortex and clearly demarcated from the surrounding normal glandular tissue. It is clear that the demonstration of tumour material in the suprarenal affords no proof that it is a neuroblastoma.

Group 3. *Ten Cases regarded as Ewing's Tumour.*—In 3 of these very careful search at autopsy revealed no evidence either of a primary carcinoma or of a tumour associated with any part of the sympathetic nervous system. In 7 cases in which autopsy was not performed very adequate material was available either in the form of the whole limb or the whole tumour. In addition, soft-tissue tumour masses have been seen subsequently in 3 cases. The histological appearances in all these cases were essentially similar. The tumours were made up of small, round, darkly staining cells the nuclei of which showed condensed chromatin. Nucleoli were rarely found. Cytoplasm was small in amount and the cells tended to lie separate from each other in a scanty stroma (*Fig.* 458). This is in marked contrast to the appearances of the reticulum cells already described, which tend to fuse together and where reticulin is abundant, whilst tumours in this group showed a striking absence of reticulin fibrils (*Fig.* 459). Areas of necrosis and hæmorrhage were

Certain authors have suggested that rosette formation may occur in Ewing's tumour (Foot and Anderson, 1941 ; Gharpure, 1941), but Lichtenstein (1952) has pointed out that in the tumours described by these authors the ' rosettes ' are composed of viable cells arranged around necrotic material, as in *Fig.* 454. In our cases pseudo-rosettes, although rare, were always obvious.

Group 4. *Four Cases which have not been given a Title.*—Two of these patients remain alive and well ten years and three years respectively after their initial symptoms. The other two died after six years and two years respectively and autopsies were not performed. These cases are grouped together

as they presented an essentially similar histological picture. In each were seen closely packed sheets of darkly staining, round cells with no evidence of necrosis or perithelial arrangement, and careful search in all cases revealed no rosettes. The cells were slightly larger and their nuclear chromatin patterns were better defined than those seen in the cases classified as Ewing's tumour. They were, however, smaller than reticulum cells and showed scantier cytoplasm (*Fig.* 463). Silver impregnation showed an amount of reticulin intermediate in quantity between Ewing's tumour and reticulum-cell sarcoma (*Fig.* 464). The appearances described here are all based on material obtained from bone and have only been compared from the point of view of cytology and histology with material similarly obtained in the other groups.

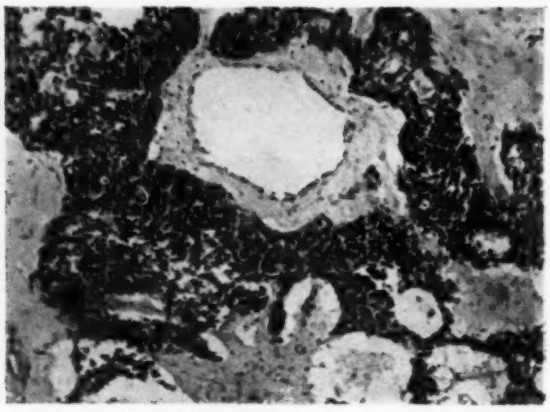

FIG. 461.—*Case* 16. A Ewing's tumour showing perithelial cellular arrangement. Hæmatoxylin and eosin. (× 86·5.)

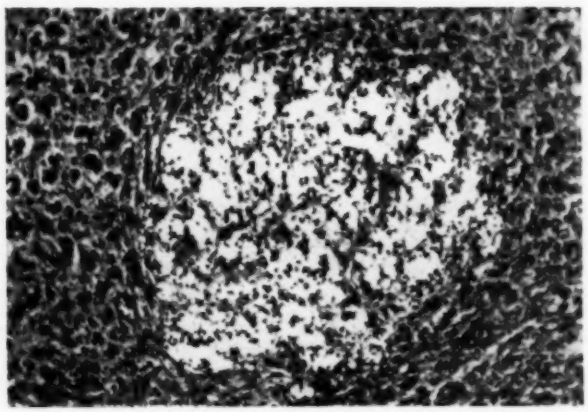

FIG. 462.—*Case* 17. A metastasis from Ewing's tumour in the suprarenal cortex. Hæmatoxylin and eosin. (× 66·6.)

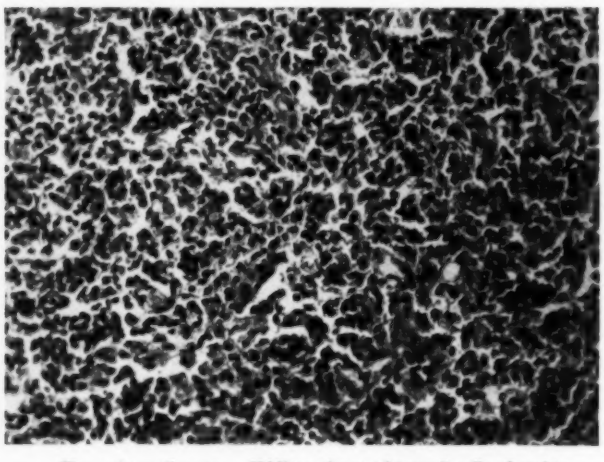

FIG. 463.—*Case* 20. Diffuse sheet of round cells showing neither perithelial arrangement nor necrosis. Hæmatoxylin and eosin. (× 175.)

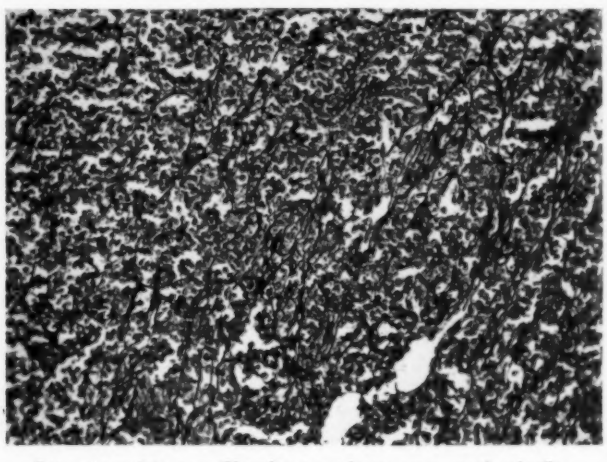

FIG. 464.—*Case* 23. Showing a moderate amount of reticulin. Silver impregnation. (× 150.)

CASE REPORTS

Group 1. Neuroblastomas.—

Case 1.—B. H., male, aged 6 years, had a lump attached to the posterior surface of the left fibula of three weeks' duration associated with a second lump in the left groin. Radiographs were suggestive of an osteogenic sarcoma and irradiation was given. After one month's treatment the initial lesion had improved but another swelling had now appeared in the upper end of the left fibula. This was also treated. Seven months after the first symptoms the child died.

Autopsy revealed multiple metastases from a round-cell sarcoma in the brain, lungs, kidneys, pelvis, and in relation to the abdominal aorta. The adrenal glands themselves were not invaded, but there was a well-defined mass of growth, macroscopically dissimilar to the other renal metastases, lying between the left kidney and adrenal. The histological appearance of these masses showed round-cell tumours with numerous rosettes. The diagnosis of neuroblastoma of inter-renal origin was therefore made.

Case 2.—T. W., male, aged 11 years, complained of pain and swelling of the right knee together with tenderness over the upper end of the right tibia. Radiographs suggested osteogenic sarcoma (*Fig.* 465) and a biopsy was performed which showed a round-cell tumour with no rosettes. Supervoltage irradiation was given. One year and two months after the initial symptoms the patient died with multiple metastases.

At autopsy there was a large tumour in the skull, a second tumour in the right mandible, and multiple tumours in the lungs and in the mediastinum in relation to the thoracic portion of the sympathetic chain. There was no tumour anywhere in the abdomen. The histology of the tumours in the chest showed multiple rosettes typical of neuroblastoma (*Figs.* 451–453).

Case 3.—R. H., male, aged 19 years, complained of pain near the right greater trochanter. Radiographs

showed no abnormality. Three months later the pain increased in severity and there was a loss of 1 st. in weight. A hard, tender tumour then appeared at the upper end of the femur. There was considerable limitation of movement and wasting of the quadriceps muscles. A biopsy showed a round-cell tumour with no evidence of rosettes. A diagnosis of Ewing's tumour was made, though the possibility of a metastatic neuroblastoma or a metastasis from a bronchial carcinoma was considered. Treatment with supervoltage irradiation was given, but pulmonary metastases appeared and the patient died eleven months after the initial symptom.

FIG. 465.—*Case* 2. Radiograph of a neuroblastoma showing a lesion of the tibia suggestive of an osteogenic sarcoma.

FIG. 466.—*Case* 7. Radiograph of a reticulum-cell sarcoma showing marked periosteal reaction more suggestive of an inflammatory lesion.

FIG. 467.—*Case* 9. Radiograph of a reticulum-cell sarcoma showing a cystic and trabeculated lesion in the humerus.

At autopsy multiple metastases were found in the lungs, ribs, and spine. A tumour was found arising from the lumbar sympathetic chain which showed the rosette formations of a neuroblastoma.

Case 4.—B. C., male, aged 18 years, complained of pain and swelling of the left thigh and knee of six months' duration, associated with a firm, smooth mass, arising from the anterior and inner part of the upper end of the left femur. There was a smaller mass above the pubis and left iliopubic ramus and rectal examination revealed a mass in front and to the left of the rectum fixed to the left side of the pelvis. Radiographs showed complete destruction of the left iliopubic ramus and almost complete destruction of the ischiopubic ramus. A biopsy was performed which showed a round-cell malignant tumour with rosette formation typical of a neuroblastoma. He was treated with irradiation, but died with metastases in the skull and chest one year after the onset of the initial symptoms.

Case 5.—E. K., male, aged 4 months, was admitted with an enlarging swelling in the preauricular region. A biopsy was performed from this bony mass and one month later a lymph-node in the neck was excised. Histology from both lesions showed a round-celled tumour without rosettes. The original lesion was treated with teleradium. Four months later, however, it increased in size and a second tumour appeared in the skull together with a left-sided pleural effusion, and tumour deposits in the ribs. Further irradiation therapy was given with little result. The tumours increased in size and number and the patient died nine months after the initial symptom.

At autopsy tumours were found in the ribs and in the cervical glands and there was a mass, 3 cm. in diameter, related to the cœliac plexus. This mass had invaded the pancreas. The suprarenals appeared normal. Histological examination of the abdominal mass and in particular of the cervical glands showed appearances typical of neuroblastoma with well-marked rosette formation.

Group 2. Reticulum-cell Sarcomas.—

Case 6.—D. S., male, aged 23 years, complained of pain in the upper end of the left femur of five months' duration and of swelling present for ten days. On admission he was wasted and ill with a swollen left leg and a mass in the left iliac fossa. High-voltage irradiation produced little change and he died one year and two months after his initial symptoms.

At autopsy a large, white tumour was found destroying the upper end of the femur and invading the soft tissues. The inguinal glands were invaded and the tumour extended into the pelvis to fill the left iliac fossa. In front of the aorta there was another mass of tumour. There were no intrathoracic metastases. There was no evidence of any tumour associated with the sympathetic nervous system, and careful search revealed no occult carcinoma. The histology of the tumour masses showed the appearances of a reticulum-cell sarcoma (*Fig.* 456).

Case 7.—B. R., female, aged 49 years, complained of pain and swelling above the right knee of three months' duration. Radiographs were suggestive of osteomyelitis of the lower end of the femur and she was treated with penicillin. There was little change in her condition for eight months, when the pain began to increase and an enlarged gland appeared in the right groin. Histology showed a reticulum-cell sarcoma. Radiographs showed

FIG. 468.—*Case* 13. Radiograph of a Ewing's tumour showing a lesion in the humerus with 'sun-ray' spicules and 'onion peel' layers.

areas of destruction throughout the right femur with well-marked periosteal new-bone formation (*Fig.* 466). The right leg and right inguinal glands were treated with high-voltage irradiation with a good initial result. However, she died four months later after a total illness of two and a half years.

Case 8.—D. K., female, aged 62 years, complained of a lump over the left sternoclavicular joint. A biopsy from the mass showed a reticulum-cell sarcoma which was treated with high-voltage irradiation. Nine months after the presenting symptom destruction of the upper part of the left tibia was noted. This was followed two months later by a similar lesion in the right ulna. These were also treated by high-voltage irradiation. One month later ulceration of the left tonsil occurred and enlarged glands appeared on both sides of the neck. Teleradium therapy was given without effect and the patient died after a total illness of seventeen months.

At autopsy there was evidence of generalized tumours of lymphoid tissue involving principally the cervical, mediastinal, and abdominal lymph-nodes. There was no evidence of any primary tumour of the sympathetic nervous system, and careful search revealed no occult primary carcinoma. Histology showed a reticulum-cell sarcoma.

Case 9.—L. R., male, aged 42 years, injured his right arm and radiographs showed a pathological fracture of the right humerus. A biopsy showed a round-cell tumour with no evidence of rosette formation. Two months later there was diffuse, firm swelling involving the upper half of the arm. Radiographs showed an extensive osteolytic lesion of the upper end and head of the right humerus (*Fig.* 467). A further biopsy showed a round-cell tumour made up of sheets of reticulum cells (*Figs.* 455, 457). High-voltage irradiation was given with excellent results. The patient is quite well two and a half years after his initial symptoms.

Group 3. Ewing's Tumours.—

Case 10.—H. E., male, aged 21 years, complained of pain and swelling of the left ankle for several weeks. This was thought to be inflammatory in origin. A biopsy showed a round-cell tumour without evidence of rosettes. He received a course of supervoltage irradiation prior to disarticulation of the hip. He recovered from the operation, but multiple metastases appeared in the lungs and he died ten months after the initial symptoms.

At autopsy the amputation site was well healed but there were multiple metastases throughout the left lung. The adrenal glands were normal and there was no evidence of tumour in relation to the sympathetic nervous system. Careful search revealed no occult carcinoma. The histology was that of a round-cell sarcoma with perithelial arrangement and no evidence of rosette formation.

Case 11.—L. C., female, aged 13 years, complained of recent increase in size of a hard, fixed swelling over the medial side of the left fibula, which she stated had been present for five years. Radiographs suggested an osteogenic sarcoma. A biopsy showed a round-cell tumour with a marked perithelial arrangement of the cells and no evidence of rosettes. High-voltage irradiation produced little change and she died six months after the initial symptom.

Case 12.—B. L., female, aged 14 years, complained of pain in the right hip radiating down the leg. A swelling appeared in the buttock extending around into the abdomen, associated with fracture of the hip. Radiographs showed destructive changes in the right ileum, sacrum, and fifth lumbar vertebra. A biopsy showed a round-cell tumour with perithelial arrangement of cells but no rosettes. Supervoltage irradiation produced a satisfactory initial response, but the patient died with multiple pulmonary metastases one and a half years after the initial symptoms.

Case 13.—M. E., male, aged 9 years, complained of increasing pain above the left elbow related to a hard, firm, fusiform swelling at the lower end of the left humerus. Radiographs revealed a tumour suggestive of an osteogenic sarcoma (*Fig.* 468). A biopsy was performed which showed a round-cell tumour consisting of small, darkly staining cells with a perithelial arrangement. Rosettes were not observed. Supervoltage irradiation was given, and six months after the initial symptoms a disarticulation of the shoulder was performed and histological confirmation of the biopsy obtained (*Fig.* 469). Four months later there was a recurrence at the amputation site. A further course of supervoltage irradiation was given, after which the tumour was removed together with half the clavicle. Recovery was uneventful, and he remains alive and well two years after his initial symptom.

Case 14.—I. C., male, aged 20 years, complained of pain in the right shoulder of four months' duration. Radiographs revealed a tumour arising from the third right rib posteriorly, causing bone expansion and cystic change. Thoracotomy was carried out and the tumour deemed inoperable. A biopsy showed a round-celled tumour with marked perithelial arrangement. No rosettes were seen. Three months later there were palpable glands in both axillæ. He was treated with supervoltage irradiation, but died nine months after the initial symptom.

Case 15.—W. C., male, aged 20 years, complained of pain and swelling at the posterior part of the left humerus. Radiographs suggested an osteogenic sarcoma, but a biopsy showed a round-cell tumour with a marked perithelial arrangement of the cells and extensive necrosis. No rosettes were observed (*Fig.* 460). The patient developed pulmonary metastases four months later and died six months after the initial symptoms.

Case 16.—B. L., male, aged 22 years, complained of pain, swelling, and weakness of the left ankle of fourteen months' duration. Osteomyelitis was diagnosed and the leg immobilized with no improvement. A biopsy was performed but was inconclusive. It was then decided that the ankle would always be useless and a below-the-knee amputation was performed. Histology showed a round-cell tumour of the lower end of the tibia, with no evidence of rosette formation but with marked perithelial arrangement (*Figs.* 459, 461). Post-operatively some inguinal glands increased in size and a block dissection was performed. They showed similar histology to the bone tumour. High-voltage irradiation was given to the groin. The patient is alive and well three years after the initial symptoms.

FIG. 469.—*Case* 13. A giant section of the humerus showing the tumour at the end of the bone and showing many surviving cells after supervoltage irradiation (6000 r) in a Ewing's tumour. Hæmatoxylin and eosin. (× 8·7.)

Case 17.—R. C., male, aged 14 years, complained of pain and swelling over the left fibula. A biopsy showed a round-cell tumour with no evidence of rosette formation. The lesion was treated with high-voltage irradiation with considerable improvement. Five months later metastases appeared in the ribs and in the lungs. The patient's condition deteriorated and death occurred four months later.

At autopsy deposits were found in the skull, ribs, lungs, and liver, and multiple deposits were seen in each suprarenal cortex which had the appearances of metastases (*Fig.* 462). Careful search revealed no primary tumour in the sympathetic nervous system and no occult primary carcinoma was found.

Case 18.—V. S., female, aged 2 years, had pain and swelling over the upper end of the left tibia. Radiographs showed the presence of a tumour in the leg and lesions in the chest highly suggestive of pulmonary metastases. A biopsy showed a round-cell tumour.

FIG. 470.—*Case* 20. Radiograph showing a destructive lesion at the lower end of the left femur.

There was no convincing evidence of rosette or perithelial arrangement but only the biopsy material was available. The patient died with multiple metastases one year after the initial symptoms.

Case 19.—J. C., female, aged 9 years, was first seen complaining of pain and swelling in the arm for three months. A tender, bony, hard tumour was found in the middle of the shaft of the right humerus. There were no other abnormalities at this time. A clinical diagnosis of Ewing's tumour was made and supervoltage irradiation therapy was instituted. After the treatment the swelling was greatly diminished and a biopsy showed necrotic debris only. The patient was discharged after two months and she remained at home for a further seven months, when she was readmitted. At this time multiple bony tumours were present. Vitamin B_{12} injections were given without effect and she died after a total illness of fourteen months.

At autopsy the cause of death was found to be terminal bronchopneumonia. There were multiple osteolytic tumours in the skull and a large tumour measuring 8 cm. in diameter was found arising from the left seventh rib

posteriorly. A tumour was found in the right ileum which extended into the pelvis, and there was a large mass in the mid-zone of the right humerus which had caused a pathological fracture. Soft-tissue tumours were found in the para-aortic and cervical lymph-nodes, and there was a small metastasis in the left suprarenal cortex. Careful search revealed no evidence of any primary epithelial neoplasm or of any tumour associated with the sympathetic nervous system. All the bony tumours were soft in consistency and greyish in colour. Histology from all areas revealed a round-cell tumour with marked tendency to perithelial arrangement and focal necrosis, but with no evidence anywhere of rosettes.

Group 4. Unclassified.—

Case 20.—M. T., female, aged 26 years, gave a history of pain and swelling of the left knee for two years. Radiographs showed a progressive destructive lesion at the lower end of the left femur (*Fig.* 470). A biopsy showed a round-cell tumour. Three months later a mid-thigh amputation was performed, and six months after that, glands which appeared in the left groin were removed. Histology from these specimens showed tumours made up of closely packed, small, darkly staining round cells with no evidence of perithelial arrangement or rosettes (*Fig.* 463). Subsequently she developed tumour masses in the lungs diagnosed by radiographs, nine and sixteen months later. These disappeared following irradiation. She remains well ten years after her initial symptoms.

Case 21.—M. C., male, aged 12 years, complained of a swelling over the upper end of the right tibia which had subsided and recurred twice during an interval of nine months. A biopsy showed a round-cell tumour without evidence of rosettes or perithelial arrangement. Irradiation was given but a pulmonary metastasis appeared sixteen months later which was also irradiated with good results. One year later another metastasis appeared in the right ilium which also responded to radiotherapy. Death occurred six years after the initial symptoms from multiple metastases.

Case 22.—P. H., male, aged 19 years, suffered increasing pain in the left thigh and calf thought to be of tuberculous origin. It was treated by immobilization, but four months later radiographs showed a neoplasm in the left greater trochanter. A biopsy showed a round-cell tumour with no evidence of rosette formation or perithelial arrangement. He was treated with supervoltage irradiation with satisfactory results and is alive and well at the present time three years after his initial symptoms.

Case 23.—D. V., male, aged 15 years, complained of pain in the backs of his thighs for eighteen months and weakness of his legs for one month. On admission he was very ill, unable to stand, and incontinent of urine. Rectal examination revealed a mass attached to the sacrum. Radiographs showed an osteolytic lesion arising from the second sacral segment. A biopsy was performed and showed a tumour made of small, darkly staining, closely packed round cells with no evidence of perithelial arrangement or rosette formation. He was treated by supervoltage irradiation with little effect, and he died with multiple metastases after a total illness of two years.

DISCUSSION

The difficulties encountered in making an exact diagnosis on biopsy material from the round-cell tumours of bone under discussion are considerable. If the true rosettes of a neuroblastoma or typical reticulum cells are seen, a diagnosis can be made with reasonable confidence, but the identification of Ewing's tumour depends partly on negative findings and on the exclusion of other conditions.

Since the original description by Ewing in 1921 a large and controversial literature has accumulated on the subject of this tumour. In the light of present knowledge much of this work will not bear critical examination. Large numbers of cases were described where the authors accepted without question the claim that the physical and radiological picture was pathognomonic, and it was largely the work of Colville and Willis (1933) and Willis (1940) which demonstrated the fallacy of this view and showed the vital importance of carefully conducted autopses. This has been emphasized more recently by Lichtenstein and Jaffe (1947), and it is indeed remarkable how few exhaustive post-mortems on cases of round-cell bone tumours have been adequately described. Among these may be mentioned 1 by Gharpure (1941) and 4 by Lichtenstein and Jaffe (1947). To these a further 9 have been added in this communication, consisting of 4 cases of neuroblastoma, 2 cases of reticulum-cell sarcoma, and 3 cases of Ewing's tumour. It is thought to be particularly significant that in two of our cases of Ewing's tumour (*Cases* 17 and 19, *Fig.* 462) undoubted metastases in the suprarenal cortex were found. It is obvious that in order to establish the manner of spread and progress of this tumour a very large number of carefully performed autopsies must be collected. Willis (1953) has suggested that all cases diagnosed as Ewing's tumour are in fact examples either of reticulum-cell sarcomas, metastatic neuroblastomas, or metastatic carcinomas which have been misdiagnosed. It is fully realized and accepted that many cases of neuroblastoma have been incorrectly labelled Ewing's tumour, and even in cases where an autopsy has been performed insufficient attention has been paid to the possibility of their extra-suprarenal origin. It is considered, however, after a careful review of the literature and the cases in our series that a group of primary round-cell tumours of bone does exist which justifies separation. Although modern investigations have shown conclusively that the criteria originally laid down by Ewing are inaccurate, we are in agreement with Lichtenstein (1952) that it is proper to retain his name in connexion with this tumour, as he was the first to describe it fully.

The characteristic histological patterns found in the cases of this series, which have been listed under Group 3 and called Ewing's tumours, are associated with the tendency to undergo necrosis and to produce the picture of a perithelial arrangement (*Figs.* 460, 461). Whilst recognizing that this feature is not in any way an indication of the manner in which the tumour is formed, it was found to be sufficiently constant to be helpful in diagnosis. Silver impregnation techniques reveal a complete absence of reticulin in the cellular areas of the tumours in Group 3 (*Fig.* 459).

The cases which have been classified in Group 4 present an interesting problem. They do not show any marked tendency to cellular necrosis and perithelial arrangement and therefore it seems justifiable to describe their cytology in detail. Cell size is intermediate between the cases found in Group 3 (Ewing's tumours) and typical reticulum cells. In brief, it has been our impression that tumours in this group present a histological picture midway

between the characteristic reticulum-cell sarcoma and the tumours in Group 3 (*Figs.* 463, 464).

This group raises the question of the relationship of Ewing's tumour to reticulum-cell sarcoma. At the present time insufficient proof exists as to the origin of Ewing's tumour to make any dogmatic statement. The most reasonable theoretical possibility seems to be that both tumours originate from primitive mesenchymal cells and represent a close but divergent line of differentiation from these cells. In this we found ourselves in general agreement with the views expressed by Oberling (1928) and by Lichtenstein (1952), and to a lesser extent with those of McCormack, Dockerty, and Ghormley (1952), for we do not consider that Ewing's tumour is a less differentiated form of reticulum-cell sarcoma.

Finally it is important to make an attempt to lay down clearly the values and limitations of the results that can be obtained from bone biopsy in the tumours under discussion :—

1. One of the histological features which can be considered diagnostic is the demonstration of rosettes which makes the diagnosis of neuroblastoma certain. It has been stressed already, however, how frequently neuroblastomas are seen where no rosettes can be found in bone biopsy specimens.

2. When sheets of typical reticulum cells and the characteristic reticulin pattern are seen the diagnosis of reticulum-cell sarcoma can be made.

3. Perithelial arrangement with necrosis cannot be regarded as a specific property of Ewing's tumour, but, in the absence of positive evidence of neuroblastoma or of reticulum-cell sarcoma, it should suggest the diagnosis.

4. Biopsy specimens are seen occasionally which show an anaplastic round-cell tumour with no characteristic features.

SUMMARY

1. Twenty-three cases of round-cell tumours of bone are presented from Westminster Hospital records. Cases of metastatic carcinoma and myeloma (plasma-cell tumours) are excluded.

2. The differential diagnosis between metastatic neuroblastoma, reticulum-cell sarcoma, and Ewing's tumour is discussed.

3. Evidence is presented to substantiate the contention that a primary round-cell tumour of bone does exist which can be differentiated from myeloma and reticulum-cell sarcoma. For this it is considered correct to retain the title of Ewing's tumour.

4. Criteria for diagnosis by means of bone biopsy are discussed, and it is stressed that in many cases a positive diagnosis can only be made at autopsy and even then it is essential for the examination to be made with great care.

5. It is considered that the present state of ignorance of the natural history and pathology of round-cell tumours of bone is due largely to a lack of post-mortem material.

We are indebted to Sir Stanford Cade for his advice and for all the clinical material he has placed at our disposal. We wish to thank Dr. I. M. Anderson and Mr. E. P. Brockman for clinical data; Dr. Peter Kerley for the radiographs; Dr. A. D. Morgan and Dr. J. G. Humble for pathology reports; and Dr. Peter Hansell and Mr. E. V. Willmott for photographs.

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URINARY STEROID RESPONSE TO OPERATION

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In recent years considerable interest has been aroused in the metabolic reaction of the body to trauma, particularly that due to surgery. By means of balance studies and chemical and isotopic analyses much valuable information has been gained concerning electrolyte, fluid, carbohydrate, nitrogen, and fat utilization in the immediate post-operative days; this has enabled the surgeon to recognize or prevent metabolic abnormalities with greater precision than was previously possible. The mechanisms by which these widespread changes occur in the cells and tissue fluids remain obscure, although many investigators have suggested that the chain of reaction passes from the damaged tissue via the hypothalamus to the pituitary (Harris, 1951), which increases its secretion of ACTH; this circulating hormone stimulates the adrenal cortex to produce more corticosteroids. These latter, it is held (Thorn, Jenkins, Laidlaw, Goetz, Dingman, Arons, Streeten, and McCracken, 1953), influence the cell enzyme systems, either directly or by controlling their substrates or co-factors. It is evident, however, that a reliable method of steroid assay is needed to study the relationship of the adrenal cortical hormones to the other more recognized metabolic changes, and one factor which has limited our understanding of the steroid response has been the absence of a method of assay which could be reasonably adopted for clinical use. Biological tests are used for the analysis of gluco- and mineralo-corticoids (Dorfman, 1954), but their application must of necessity be limited to those substances which show biological activity; these only present as a small fraction of the total urinary steroids. Although paper chromatography presents an elegant method for urinary or plasma analysis, it has not been sufficiently developed to allow a simple quantitative steroid assay.

For the chemical estimation of the steroid response to surgery either plasma or urinary samples may be utilized. Nelson and Samuels (1952) described a technique for the estimation of the plasma-steroids which are present in small quantities, chiefly in an unconjugated 'free' form; it determines those cortical steroids with a 17, 21 dihydroxy-20-ketone group, such as hydrocortisone, cortisone, and Reichstein's compound S and their hydrogenated derivatives, but does not measure the conjugated forms. The technique consists of a chromatographic separation of the plasma-steroids, followed by the colorimetric determinations of the eluted compounds; it is, however, not free from difficulties. Sandberg, Eik-Nes, Samuels, and Tyler (1954) suggested that the plasma level of 17-hydrocorticosteroids in normal subjects is 3–22 μg./100 ml.; Franksson, Gemzell, and von Euler (1954) 4–10 μg. in a group of pre-operative patients, and Klein, Papadatos, Fortunato, and Byers (1955) 11 μg. The maximal blood-level in patients undergoing surgery is given as $31{\cdot}4 \pm 1{\cdot}9$ μg./100 ml. (Franksson and others, 1954) while Klein and others (1955) found the average rise in 19 patients to be 51 μg.

The development of urinary methods for steroid estimations is hindered by the form in which steroid excretion is carried out; for whereas in the plasma the steroid is predominantly in the 'free' and active form, in the urine steroids are mainly conjugated as biologically inactive glucuronides and sulphates. Assays which depend on the hydrolysis of conjugates to a 'free', and therefore more easily assayed material, are not completely successful and only partially reflect adrenocortical activity (Norymberski, Stubbs, and West, 1953).

Norymberski (1952) demonstrated that sodium bismuthate converts in situ those steroids (17-ketogenic) bearing the side chains 17 : 20 : 21-triol, 17 : 21-diol-20-one, 17 : 20-glycol to 17-keto-steroids, which can then be hydrolysed, extracted, and assayed by a modification of the well-established Zimmermann method. The reliability of this assay of urinary 17-ketogenic steroids as an assessment of adrenocortical activity has been reviewed by Norymberski, Stubbs, and West (1953) and Hubble (1955).

PLAN OF STUDY AND TECHNICAL METHODS

The general purpose of this investigation was to find out the pattern of corticosteroid response to a standard operation. For this purpose we have used the Norymberski assay of urinary 17-ketogenic steroids. The results can only be interpreted in a general way as no detailed analysis of individual steroid components will be described in this paper, nor can it be assumed that the plasma-steroid level bears a direct relationship to the urinary excretion pattern either in magnitude or in duration. This method does, however, enable us to define a urinary steroid response to operation, and this it is hoped will finally be integrated with the more recognized electrolyte and nitrogen metabolic response to surgery, such as that described in detail by Moore and Ball (1952), Moore (1954), and Black and Jepson (1954).

All our patients were men whose ages ranged from 17 to 76 years. Four of the patients presented with a long history of duodenal ulceration but without any evidence of stenosis, recent weight loss, or metabolic imbalance. These patients were studied in order that operative response could be established in individuals uncomplicated by previous gross metabolic disturbances. Four patients, in addition to the history of chronic duodenal ulcer, presented with visible peristalsis and a long history of vomiting. Where the patient showed gross clinical or biochemical evidence of electrolyte or water deficiency, this was corrected as far as possible prior to operation (Black and Jepson, 1954). A further patient who underwent a simple laparotomy for advanced gastric carcinomata and who does not fall into either of these two groups, will be described in some detail. Reference will also be made to some studies prepared on two patients who had previously undergone

lilateral adrenalectomy for advanced mammary carcinoma.

Before operation the patients were placed on a light diet for 48 hours; on the day of operation no fluids were given and thereafter milk mixture supplemented with protein and electrolytes was given for about a week. Urine was collected in 24-hour specimens usually for 4 days prior to the operation and for varying periods up to 10 days following. It was stored in a refrigerator without preservative until analysis. The operation in the 8 cases of duodenal ulcer consisted of a partial gastrectomy, ante- or retro-colic, performed under general anæsthesia by the same surgeon (R. P. J.). The duration of the operative period was 1–1½ hours and no intravenous therapy was required during or following the procedure, which was standardized as far as was possible, both in respect of surgical technique and anæsthesia.

The post-operative course of the patients undergoing partial gastrectomy was uncomplicated. The detailed technique of the steroid assay was that of Norymberski (Norymberski, Stubbs, and West, 1953; Gibson and Norymberski, 1954). A summary of the presentation of the steroid assays given in the tables and text is as follows: the figures in parenthesis are excretions of ketosteroids or ketogenic steroids corrected by reference to the creatinine excretion. The correction is made as follows: for each day an 'adjusted' excretion is obtained, viz.:

$$R_{adj.} = R_{obs.} \times \frac{C_{mean}}{C_{obs.}}$$

where $R_{adj.}$ is the 'adjusted' excretion, $R_{obs.}$ is the observed ketosteroid or ketogenic steroid excretion and $C_{obs.}$ is the observed creatinine excretion for the day in question, and C_{mean} is the mean daily excretion of creatinine for the period of the correction. Finally, from the 'adjusted' excretion is obtained the corrected excretion:—

$$R_{corr.} = R_{adj.} \times \frac{R_{mean}}{R_{adj.\ mean}}$$

where $R_{corr.}$ is the corrected value sought, R_{mean} is the mean daily excretion of ketosteroid (or ketogenic steroid) for the period in question, and $R_{adj.\ mean}$ is the mean of the 'adjusted' excretions calculated as above.

URINARY STEROID EXCRETION OF PATIENTS IN PRE-OPERATIVE METABOLIC BALANCE

The results of the urinary steroid estimations on the 4 patients without a history of gross weight loss or vomiting are given in *Table I*. The urinary ketogenic steroid excretion prior to operation varied from 6·4 to 12·9 mg./24 hr. These values are somewhat lower than the range for normal males, which is given by Norymberski and others (1953) as 9·6–19·2 mg./24 hr., but fall within the range accepted in this laboratory (Levell, Mitchell, Paine, and Jordan, 1955). Following partial gastrectomy there was a marked increase in ketogenic steroid excretion, which was maximal on the first post-operative day, gradually declining to the pre-operative range over the succeeding 3–7 days. An illustrative case is shown in *Fig.* 471. In three of the four patients urine collection was maintained for 7–9 days post-operatively, and in this period the 24-hour urinary steroids did not fall significantly below the pre-operative values. The maximum increase in 24 hours' excretion following operation varied greatly from patient to patient, being 52·8 mg./24 hr. in G. W. (aged 69), 47·7 mg. in M. B. (aged 17), 24·7 mg. in H. H. (aged 52), and 11·2 mg. in H. B. (aged 76). No variation in operative procedure or post-operative course could be found to account for this. If the total ketogenic excretion for the 4 days following operation is compared with the 4 days preceding (either observed or calculated from the mean figures), the cumulative balance brought about by the operation is + 93·3 (G. W.), + 101·8 (M. B.), + 2·4 (H. B.), and + 31·2 (H. H.) mg.: this again reflects a wide variation in ketogenic steroid response from individual to individual.

The range of 24-hour ketosteroid excretion pre-operatively was 5·5–12·0 mg. In patients G. W. and M. B. the 24-hour ketosteroid excretion was increased for the first 4 post-operative days, while in M. B. and H. H. no change was detected. This variability of ketosteroid response to operation has been previously noted (McPhee, 1953; Moore, 1954). A 4-day balance of ketosteroids prior to and following operation results in + 43·7 mg. (G. W.), + 18·7 mg. (M. B.), −14·9 mg. (H. B.),

Table I.—URINARY STEROID EXCRETION OF PATIENTS IN PRE-OPERATIVE METABOLISM BALANCE

(K.S. = 17-ketosteroids; K.G.S. = 17-ketogenic steriods expressed in mg./24 hr. throughout; O = operation.) Figures in parenthesis are corrected, as described in the text. Creatinine in grammes.

Day	G. W.		M. B.			H. B.			H. H.	
	K.S.	K.G.S.	Creatinine	K.S.	K.G.S.	Creatinine	K.S.	K.G.S.	K.S.	K.G.S.
−4	6·6	7·6	2·4	8·9	12·5					
−3	6·8	7·3	2·5	8·2	12·8					
−2	5·5	6·4	3·1	10·4	9·5	2·6	8·2	9·2	11·5	12·9
−1	7·5	9·1	2·0	8·0	11·4	2·5	7·8	8·7	12·0	13·7
O										
+1	20·1	52·8	2·5	13·8	47·7	0·9	2·3 (4·3)	7·6 (11·2)	10·2	24·7
+2	21·2	33·1	0·5	2·5 (13·6)	7·4 (36·5)	0·3	0·7 (3·9)	2·4 (10·8)	10·8	20·5
+3	8·4	17·3	4·8	21·9 (10·8)	53·1 (24·0)	3·5	9·9 (4·7)	19·2 (7·2)	12·6	17·6
+4	20·4	20·5		16·0	39·8	2·6	4·2	9·0	16·4	21·6
+5				6·4	18·0	2·3	5·2	7·7	10·4	14·6
+6				10·2	19·9	2·3	7·6	9·1	14·3	24·2
+7				5·8	9·6	2·5	9·1	10·0	6·3	9·2
+8				7·5	12·4	2·1	10·0	7·6	13·5	14·0
+9							7·6	8·1		

and + 13·0 mg. (H. H.) (*Fig.* 472). Although the post-operative excretion of urinary keto and ketogenic steroids did not run parallel, the patients G. W.

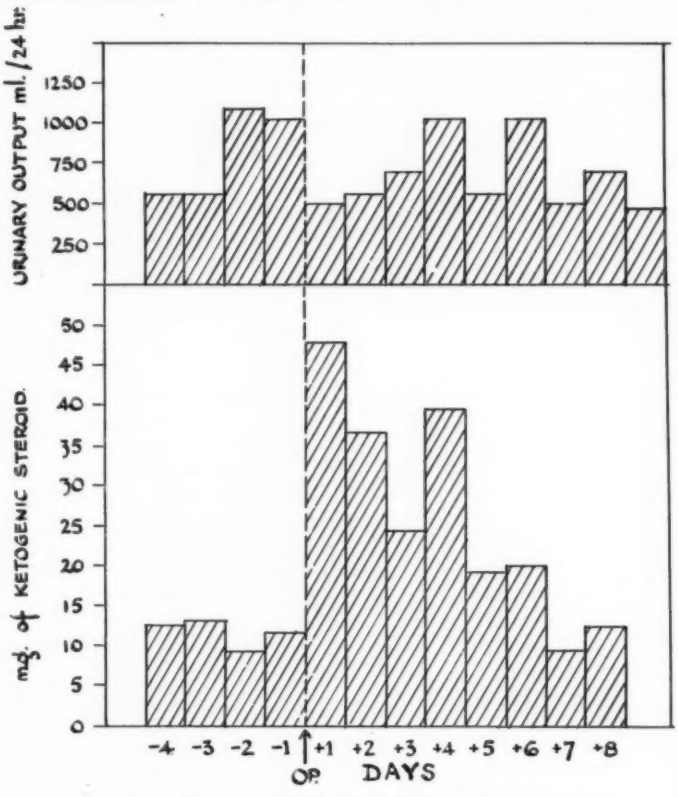

FIG. 471.—Patient, M. B., showing effects of partial gastrectomy on urinary volume and ketogenic steroids.

and M. B., who demonstrated the most marked ketogenic response, also had the highest ketosteroid excretion.

URINARY STEROID EXCRETION OF PATIENTS IN PRE-OPERATIVE METABOLIC IMBALANCE

Four patients, M. S. (aged 42), J. S. (aged 67), E. O. (aged 58), and E. G. (aged 36), presented with a history of duodenal ulceration culminating in clinical pyloric stenosis with repeated vomiting. They all showed evidence of water and electrolyte deficiency. The pre-operative 24-hourly ketogenic steroid excretion was similar to the 'normal' group and varied from 7·3 to 19·2 mg. The ketogenic urinary output post-operatively was maximal in the first 24 hours in M. S. In J. S. and E. O. the maximal value was seen in the second 24-hour period. This could possibly be explained in the case of J. S. by the marked oliguria (120 ml.) which occurred in this period. In the case of E. G. no increase of ketogenic steroid excretion was noted following the operation; this patient will be discussed in more detail later in this paper. In the three patients, M. S., J. S., and E. O., who demonstrated a ketogenic response to excretion, the cumulative balance for the 4 post-operative days compared with the 4 pre-operative was 65·6, 86·1, and 126·0 mg. respectively (*Fig.* 472). In the patient M. S. the excretion of ketogenic and ketosteroids on the 7–9 post-operative days fell significantly below the pre-operative level; this phenomenon has previously been noted for ketosteroid excretion (McPhee, 1953).

In two of the patients, E. O. and E. G., an infusion (i.v.) of 25 units ACTH in 500 ml of saline over 6 hours was given 4 days before and 4 or 5 days after the partial gastrectomy (*Table II*). In E. O. the pre-operative ACTH resulted in a 24-hr. excretion of 29·7 mg. while a similar dose of ACTH post-operatively produced 66·6 mg.; an explanation for this could be that the adrenal gland is more responsive to the pituitary hormone in the latter period; alternatively the tissue utilization of the steroid may be suppressed temporarily so that a constant adrenal output would cause a high plasma level and higher urinary excretion. One other finding is of interest, for although this patient's maximal 24-hr. excretion of ketogenic steroid was 51·1 mg. post-operatively, under the additional stimulation of the ACTH this was augmented to 66·6 mg. This supports the contention of Sandberg and others (1954) that the adrenals are not maximally stimulated by operations of this severity. In contrast, E. G., who gave a moderate rise (30·7 mg.) in ketogenic excretion in response to pre-operative ACTH stimulation, showed no increase in ketogenic excretion either following the partial gastrectomy or further ACTH stimulation on the fourth post-operative day. This patient, however, had a perfectly smooth convalescence with sound wound healing. Ingle (1952) has demonstrated experimentally that as long as a 'permissive' quantity of plasma-steroids is present, nitrogen and electrolyte metabolic response and tissue healing will occur. We have similar findings in humans maintained during the operative period on a constant cortisone dose, and the case of E. G. supports this contention.

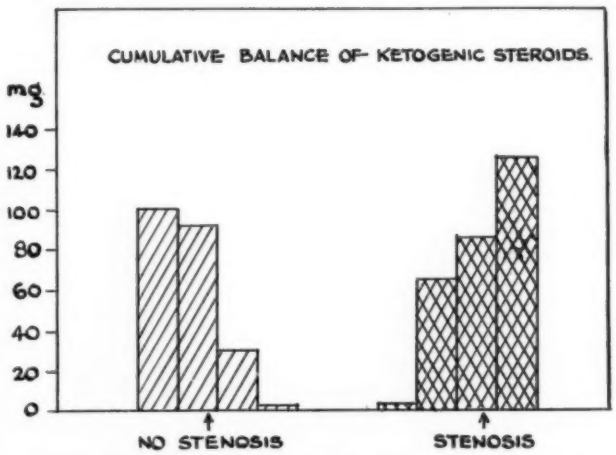

FIG. 472.—Showing cumulative 4-day balance of ketogenic steroids; in case of E. G. 3-day balance is given.

FURTHER STUDIES

Norymberski and others (1953) found that the percentage recovery rate in the urine of orally administered cortisone is in the region of 45. To

check this figure the urinary ketogenic steroids were estimated in two patients who had some months before undergone bilateral adrenalectomy and oöphorectomy for advanced carcinoma of the breast. Both patients were gaining weight and in good general condition and without evidence of any urinary impairment. Both patients were maintained on 50 mg. of oral cortisone acetate and the mean ketogenic excretion in the urine was 23 and 20 mg. respectively, figures which closely approximate to those given by Norymberski. When the oral cortisone was supplemented by a single dose of 100 mg. cortisone intramuscularly, the daily excretion figure rose to 35 and 31 mg./24-hourly; this injection in addition maintained the daily excretion at this level for at least 4 days. These patients, without any internal source of sex hormones, continued nevertheless to secrete urinary ketosteroids.

One further patient is of interest (*Fig.* 473). This man, A. B., aged 55, gave a recent history of marked weight loss and postprandial pain and was submitted to a simple laparotomy under general anæsthesia to confirm the diagnosis of an advanced gastric neoplasm, which was infiltrating the liver and colon. No further procedure was undertaken. His preoperative ketogenic steroid excretion (17·4 to 24·8 mg./24 hr.) was by far the highest in this series and outside the upper range of normal. Following the laparotomy the steroid excretion rose from 38·0 mg. in the first 24-hour period to 70·0 mg. in the fourth. Both in magnitude and the delayed rise this was an unusual type of response. The 4-day cumulative balance was 125·0 mg. for the ketogenic steroids; the total 4-day post-operative output of 205 mg. was the highest and most sustained we have observed, and one which, it is stressed, followed minor surgical trauma. In this case the magnitude of steroid

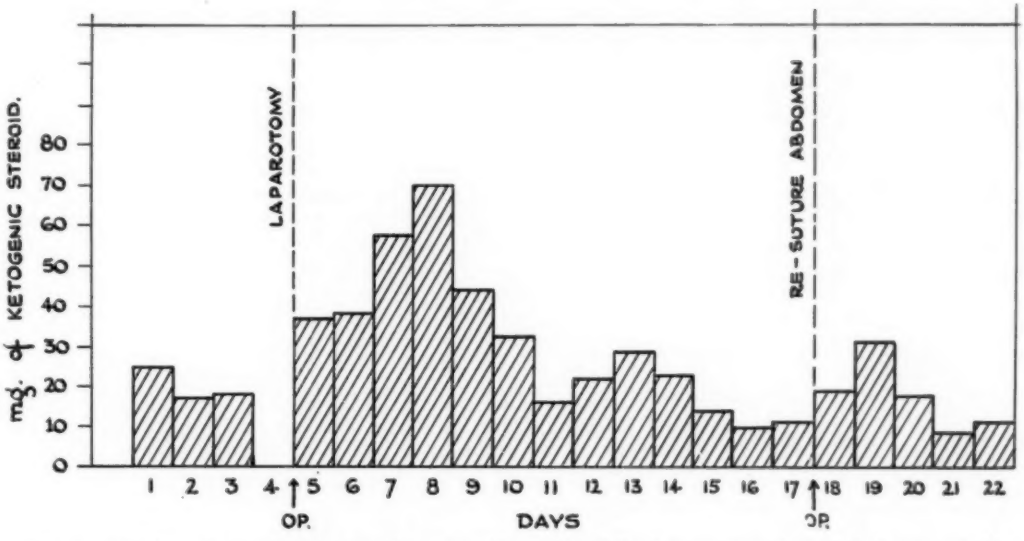

FIG. 473.—Patient, A. B., showing the urinary steroid excretion following two operations of similar magnitude.

Table II.—URINARY STEROID EXCRETION OF PATIENTS WITH CLINICAL PYLORIC STENOSIS

(K.S. = 17-ketosteroids; K.G.S. = 17-ketogenic steroids expressed in mg./24 hr. throughout; O = operation.)

DAY	M. S.		J. S.		E. O.		E. G.	
	K.S.	K.G.S.	K.S.	K.G.S.	K.S.	K.G.S.	K.S.	K.G.S.
−8					9·1	11·9		
−7					6·2	7·3		
−6					[8·5	29·7]*	9·5	12·5
−5					9·3	10·2	9·4	19·2
−4					7·8	6·3	[15·8	30·7]*
−3	11·2	10·8			6·7	4·2	8·7	26·4
−2	10·7	13·9			6·8	4·8	11·0	12·6
−1	10·5	10·1	7·4	8·2	5·9	5·5	7·7	8·3
O								
+1	17·1	42·9	3·1	9·0	4·8	38·2	6·1	8·5
+2	17·1	29·7	11·1	50·7	20·9	51·1	6·4	9·3
+3	16·3	22·0	9·0	27·5	18·8	40·7	10·7	16·2
+4	14·4	17·4	17·9	31·7	26·5	16·7	[17·0	16·0]*
+5	6·3	9·1	18·2	35·1	[20·4	66·6]*	9·5	7·6
+6	5·4	10·7	10·7	25·8	12·5	14·0	9·1	8·7
+7	4·1	6·5	4·2	15·7	10·7	18·6	7·8	16·9
+8	3·2	4·1	6·5	8·5			8·9	8·3
+9	4·7	6·9	4·9	12·6				

* = 25 units ACTH i.v.

response was not directly related to the severity of the trauma (Moore, 1954), but reflected in addition the patient's general condition, disease process, and possibly an excessive impairment of liver function. On the thirteenth post-operative day this patient completely dehisced the abdominal wound, which on examination showed no macroscopical evidence

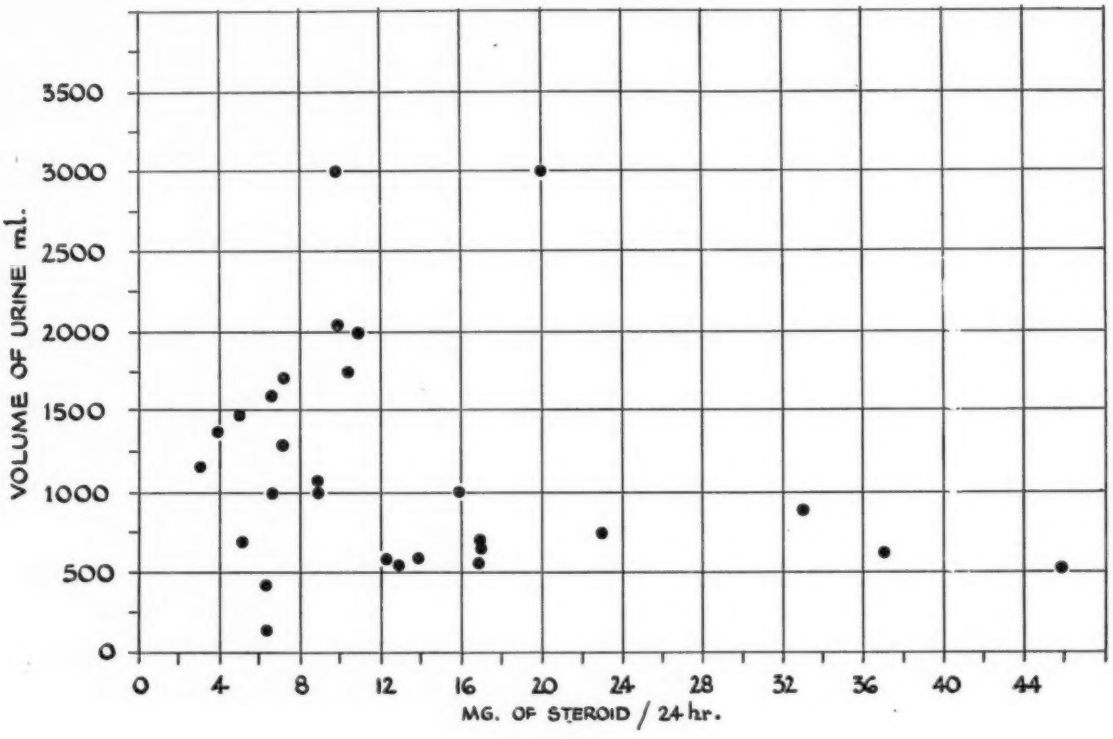

FIG. 474.

of healing. He, therefore, underwent a further general anæsthetic and wound resuture. The steroid response to the second operation was minimal, the maximal 24-hr. excretion only being 30 mg. and the 4-day cumulative balance 16·3 mg. The final resuture healed without difficulty. It has been repeatedly demonstrated that high cortisone dosage may suppress inflammatory and fibroblastic reaction and this may have occurred in this individual, in whom the 24-hr. peak excretion of 70 mg. of ketogenic steroid is approximately the equivalent of 150 mg. of cortisone acetate by mouth.

No direct correlation between urinary volume and steroid excretion could be shown (*Fig.* 474), except in case J. S., and apparently large and varying amounts of steroid compounds can be cleared by the kidneys in 24-hr. urinary volumes of 400 ml.

DISCUSSION

Evidence has accumulated in recent years to suggest that 17α-hydroxycorticosterone (hydrocortisone ; Kendall's Compound F) and corticosterone are the hormones secreted in the largest quantities by the adrenal cortex (Nelson and Samuels, 1952 ; Thorn and others, 1953 ; Eik-Nes, Sandberg, Nelson, Tyler, and Samuels, 1954). Additional steroids occur in perfusates of adrenal glands in varying amounts ; recently Simpson, Tait, and Bush (1952) have demonstrated the presence of aldosterone in adrenal gland extracts and in urine. The principal excretion product in the urine is tetra-hydrocortisone, which is both conjugated and biologically inactive (Baggett, Glick, and Kinsella, 1952). It is probable, therefore, that the ketogenic assay gives an accurate reflection of the adrenal cortical secretion in terms of hydrocortisone, cortisone, and their breakdown products. It does not estimate aldosterone, nor does it estimate corticoids with no hydroxyl at the 17 position, substances essentially concerned with electrolyte control. That changes in 17α-hydroxycorticosterone are quickly reflected in the urine, excepting possibly when a marked oliguria is present, is shown by the fact that 50 per cent of oral cortisone is excreted in the urine within the first 4 hours (Norymberski and others, 1953). Sandberg and others (1954) state that plasma levels of 17-hydroxycorticosterone rise following the induction of the anæsthesia, and increase approximately in relationship to the severity and magnitude of the operation. These authors suggest that the elevation of the 17-hydroxycorticosteroids persists for at least 6 hours after the operation ; Franksson and others (1954) give the duration as 24–72 hours. Some of the variations in the reported rise and duration of the plasma-steroids may be due partly to the small amounts (micrograms) of steroid measured : furthermore the plasma rise is partly due to impairment of hepatic function post-operatively (Tyler, Schmidt, Eik-Nes, Brown, and Samuels, 1954) and the degree to which this occurs may vary considerably.

Birke, Franksson, and Plantin (1955) described a rise in the reducing corticoids in the urine for 3 to 5 days following operation, and the urinary steroid

response to surgery was also assessed by Moore (1954), using the methods of Reddy, Jenkins, and Thorn, although exactly which steroidal configurations are measured by this method is not clear. Moore gives the normal range as 5–10 mg./24 hr. of urinary 17-hydroxycorticosteroid. This rises to 35–40 mg./24 hr. with major surgery and 15–25 mg./24 hr. following minor surgery, and persists for 3–4 days before returning to a subnormal level, where it is apt to remain for several days. He suggests the response is related to the magnitude of the trauma and the total nitrogen loss. The findings in the present paper do not entirely support these conclusions. The highest and most sustained urinary steroid excretion was found in a patient submitted to a simple laparotomy, and in many of the patients the magnitude and duration of the response seems to have been an 'individual' one and not obviously related to age or the stress of the operation. The response in 3 patients with pyloric stenosis, major weight loss and electrolyte imbalance, appears to be of a similar range to those in the normal group, although it is possible that with a larger group a significantly greater steroid excretion may become apparent in the patients with pyloric stenosis. In the fourth patient in this group (E. G.) both operative trauma and post-operative ACTH failed to produce an augmentation of urinary steroids. It is interesting to note that this man's post-operative convalescence was uncomplicated, a fact which suggests that if a 'permissive' quantity of plasma-steroid is available a normal metabolic response and repair can occur. It is possible that the clinical complications arise where the plasma-steroid level is abnormally low, such as may follow adrenal surgery, resulting in peripheral vascular failure and hypotension, or where the plasma-steroids are abnormally high (patient A. B.). In the latter case inhibition of fibroblastic activity may be an additional factor impairing wound healing.

Although it has been frequently assumed that the nitrogen changes following operative procedures are in a large part dominated by the 17α-hydroxycorticosterone secretion, this would on the present evidence seem unlikely. It is well established that post-operative negative nitrogen balance is most marked in the healthy, and less pronounced in the debilitated elderly and those patients with marked weight loss (Moore and Ball, 1952). It is difficult to reconcile these findings with the wide variations of urinary steroid excretion in normal patients, the apparently equivalent response in those with pyloric-stenosis, and the exaggerated excretion pattern of patient A. B. who was grossly debilitated. In addition, the timing of the metabolic response varies; thus the steroid response is maximal in the first two days while the negative nitrogen balance is sometimes maximal at 5–7 days, and may, following operations of the magnitude of a partial gastrectomy, go on for many weeks. If the animal findings of Ingle are translated to man a close connexion between the 17α-hydroxycorticosterone, electrolyte, and nitrogen responses to operation would not be expected, and it may be more reasonable to infer that the steroid response assayed by the Norymberski method is 'anti-inflammatory', damping down the local response to trauma or infection. We suggest, therefore, that an abdominal operation of moderate severity usually evokes a steroid response, in the form of 17-hydrocorticosterone, which is maximal on the first or second day following operation and lasts for a varying period up to 10 days post-operatively; that the magnitude of this response, although probably allied to the degree of stress inflicted by the operation, also varies greatly from individual to individual and according to the disease process; and that this type of steroid response is not essential for normal post-operative healing and convalescence.

SUMMARY

1. The urinary ketogenic steroid response to partial gastrectomy in 'normal' patients and those in biochemical imbalance is described. In addition, the response to other forms of surgery is mentioned.

2. The ketogenic response is usually maximal in the first 48 hours post-operatively and may stay above pre-operative levels for many days.

3. Evidence is put forward which suggests that the response is not directly related to the magnitude of the trauma and that normal convalescence may occur without any increased urinary secretion of ketogenic steroids.

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THE COMPLICATIONS OF GASTROSCOPY AND ŒSOPHAGOSCOPY

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THE most common complication of present-day gastroscopy and œsophagoscopy is peri-œsophageal infection resulting from damage to the mucosa of the upper œsophagus.

The usual site of injury is the posterior œsophageal wall in the post-cricoid region, where the longitudinal muscle-fibres are deficient. In this region the thin œsophageal wall may be compressed between the lower cervical vertebral bodies and the rigid portion

FIG. 475.—The sequestrum in the lower jaw in the case of osteomyelitis following gastroscopy.

of the endoscope, *particularly in subjects with anterior bony projection of the vertebræ due to osteo-arthritis.* The injury, which may be a bruising, a pressure necrosis resulting in slow perforation, or an actual splitting of the wall, results in a retro-œsophageal infection; this may spread downwards, giving rise to a superior mediastinitis, but if adequate treatment is instituted may in fact be almost entirely confined to the neck.

Lower œsophageal injury may be associated with some pre-existing local disease such as carcinoma, and the resulting mediastinal infection is often fatal.

Œsophageal injury following *gastroscopy* is reported by Schindler (1940), White (1941), Touroff (1941), Paul and Lage (1943), Freeman (1945), Paul and Antes (1946), Goligher (1948), and Boon (1951) 1 case each; also by Schindler (1950) 2 cases, by Neuhof and Jemerin (1943) 3 cases, and by Fletcher and Jones (1945) 10 cases. Hermon Taylor (1945) quotes 1 case in his large experience. Jones, Doll, Fletcher, and Rodgers (1951) found the incidence to be 50 in 49,000 gastroscopies, and also added a further 4 cases.

Of these 78 cases recorded in the literature only 7 are reported as occurring definitely in the lower œsophagus; 35 were fatal cases.

Numerous cases are on record of œsophageal trauma due to *œsophagoscopy*. Mosher (1935) gives an incidence of 19 perforations in 938 œsophagoscopies.

Gastroscopy may occasionally give rise to other complications. Perforation of the stomach was not infrequent in the days of the rigid gastroscope, and still sometimes occurs. Schindler (1950) mentions 8 cases, Avery Jones and others (1951) collected 9 cases. Boon gives an incidence in his series as 4 in 4000 gastroscopies.

Pneumoperitoneum following gastroscopy has been reviewed by Ylvisaker and Myhre (1951), who collected 11 cases from the literature and added 1 case of their own; Friedrich (1951) also reports a case. Perforation in these cases is frequently so small as to elude discovery; out of 7 cases explored surgically, in six careful examination failed to reveal the site of perforation. Pneumoperitoneum may also follow perforation of the jejunum from gastroscopy in patients who have had a gastric resection (Rumball, 1939).

A unique case of perforation by the rigid gastroscope is recorded by Schindler, in which the instrument was passed, by an assistant, down the trachea and right bronchus into the right pleural cavity. Recovery, after thoracotomy, was uneventful.

Some gastroscopists consider recent gastric hæmorrhage and œsophageal varices to contra-indicate gastroscopy, owing to the risk of causing bleeding, but in this unit a large number of both types of case have been examined without trouble. The risk of perforating an aortic aneurysm has been pointed out by Schindler and others, but there appears to be no report of such a catastrophe.

The danger of severe gastric hæmorrhage, particularly in patients with a latent hæmorrhage diathesis, was pointed out by Henning (1937, p. 29), who had met such a case. Avery Jones and others (1951) found 7 cases in their series; they also reported 1 case of acute phlegmonous gastritis, 1 of bursting of a chronic para-œsophageal abscess, and 2 cases of unexplained death a few hours after gastroscopy. They found 5 cases of severe reaction to local anæsthetic, 4 of them fatal. Henning mentions the danger of causing a flare-up of a chronic tonsillitis.

Since 1943, 7200 gastroscopies and 605 œsophagoscopies have been carried out in this gastro-enterological unit. Twenty-nine cases of damage to the upper œsophagus and 5 to the lower œsophagus have occurred. These cases are examined (*Tables I* and *V*) from the point of view of causation, prevention, diagnosis, and treatment of such lesions. The only other complication following gastroscopy which has occurred in this unit is a case of osteomyelitis of the mandible. This case is recorded on account of its rarity.

REPORT OF A CASE OF OSTEOMYELITIS OF THE MANDIBLE FOLLOWING GASTROSCOPY

A highly-strung woman aged 60 was examined with a Hermon Taylor gastroscope on Feb. 15, 1952, under local anæsthesia, during the course of investigation of abdominal pain and vomiting.

During gastroscopy the patient felt some pain in the floor of the mouth, otherwise examination proceeded normally with no difficulty in passing the instrument. No lesion was detected in the stomach.

For four days subsequently she had a small abrasion on her left lower gum; the molar and premolar teeth in this region had been extracted some time previously. The abrasion healed without treatment and caused her no further trouble until more than two months later, when she noticed pain on moving her jaw. Examination on May 19 revealed a small elongated swelling half an inch in length on the inner side of the left alveolar margin. A radiograph of the lower jaw at that time showed a localized area of rarefaction of the bone with what appeared to be a sequestrum (*Fig.* 475).

She was given a course of chloromycetin, her symptoms gradually subsided, and the soft-tissue swelling disappeared in the course of the next few weeks. Radiography on Aug. 11 showed a return to normal in the appearance of the bone.

Comment on Case.—The position commonly adopted for gastroscopy is the left lateral, with the knees and hips flexed, the left hand placed in the right axilla and the right hand grasping the edge of the table opposite the left elbow. The head is supported by a nurse, the neck being at first flexed, then gently extended as soon as the flexible part of the instrument has passed the cricopharyngeus muscle. The rigid part of the instrument usually lies in the left angle of the mouth, passing between the alveolar margins in the molar region, with the head slightly inclined to the right, but it may be placed in any convenient gap in the upper teeth, the position of the head being adjusted accordingly. In its usual position the instrument may cause a certain degree of pressure on the outer side of the upper alveolar margin or molar teeth, and on the inner side of the lower alveolar margin or molars, depending on the conformation and range of movement of the jaws.

Pressure on the *upper* jaw, usually present to a greater or lesser degree, and sometimes causing a minor abrasion, is minimized by lateral flexion of the head, combined with a small degree of rotation towards the side in which the instrument is lying. Undue extension of the neck must be avoided.

Pressure on the *lower* jaw is as a rule hardly noticeable. It can be reduced by relaxing the lower jaw. Patients occasionally feel a little discomfort in this region, but actual abrasion is rarely encountered.

In the above case, though no undue immobility of the jaw or abnormal configuration was present, a degree of pressure sufficient to cause an abrasion certainly occurred, and it seems likely that a small subperiosteal hæmatoma was produced which subsequently became infected. Restoration to practically normal bone within a few weeks makes it improbable that there was any pathological condition previously present such as a retained root.

The possibility of such a complication emphasizes the extreme gentleness required in handling the endoscope, for pressure over bone may cause damage not only to the overlying structures as in the hypopharyngeal region, but also to the bone itself.

INJURY TO THE UPPER ŒSOPHAGUS

(*Table I*)

Twenty-three cases of damage to the œsophagus in the hypopharyngeal region have occurred during the course of 7200 gastroscopic examinations made, almost without exception, with the Hermon Taylor instrument (incidence about 1 in 300). A similar lesion has occurred 6 times in 605 œsophagoscopies (incidence about 1 in 100). Definite evidence of damage is present in every case; namely the presence of gas in the tissues of the neck, or actual abscess formation. A number of doubtful cases have been excluded.

FIG. 476.—Lateral radiograph of the neck showing the retrotracheal broadening and the gas in the tissues of the neck. It also shows the anterior lipping of the cervical vertebræ which is a common feature in cases of peri-œsophagitis following endoscopy.

Predisposing Factors.—

Gastroscopic Diagnosis.—The stomach was examined in 24 cases; in 9 a normal stomach was reported, in 8 evidence of gastric atrophy, in 7 gastric ulcer. Gastric atrophy is present in only 1 case in every 20 gastroscoped, but is present in 1 in every 3 of the cases which developed peri-œsophagitis (*Table II*); it thus appears to be an important predisposing factor.

Cervical Osteophytes.—Radiography showed these to be present in 16 cases and absent in 5; in 8 cases

Table I.—DAMAGE TO UPPER ŒSOPHAGUS FOLLOWING ENDOSCOPY

Case No.	Under 50	Over 50	Diagnosis	Dysphagia	Pyrexia	Signs in Neck				X-ray Signs			Days to Onset of Treatment	Days to Operation	Days to Recovery	Result	Remarks
						Swelling	Supraclavicular Tenderness	Crepitus	Sternomastoid Spasm	Gas	Broadening	Osteophytes					
Gastroscopy:—																	
1		F.	Atrophic gastritis	+	+		+						7	8		Died (17th day)	At home for 7 days, no treatment. Abscess drained on 8th day
2		F.	Gastric ulcer	+	+	+	+	o		+			1	5	41	Recovered	Abscess drained with suction
3		F.	Atrophic gastritis + G.U.	+	+			+		+			1		24	Recovered	
4		F.	Normal stomach		+	+		+		+			<1		13	Recovered	
5		F.	Atrophic gastritis	+	+			+				+	1		5	Recovered	
6	F.		Atrophic gastritis	+	+	+				+			9	11	33	Recovered	Treated at home by her doctor for 9 days. Abscess drained 11th day
7		F.	Normal stomach	+	+	+	+	+		+			<1		8	Recovered	
8		F.	Atrophic gastritis	+	+			o	+	+	+	+	1	15	34	Recovered	Abscess drained
9		M.	Normal stomach		+			+		+	+	+	2	15	35	Recovered	Abscess drained
10		F.	Normal stomach	+	+			o	o	+	+	+	4	8	28	Recovered	Abscess drained
11		F.	Atrophic gastritis		+			+	+	+	+	+	<1		14	Recovered	
12		M.	Normal stomach		+					+	+	+	1		7	Recovered	
13	F.		Normal stomach		+		+			+	+	+	<1		10	Recovered	
14	F.		Normal stomach	+	+			o	+	+	+	o	2		15	Recovered	
15		M.	Normal stomach		+			+		+	+	+	1		12	Recovered	
16		M.	Probable atrophy	+	+		+	o		+	+	o	1	20	35	Recovered	Kyphotic. Neck drained. No pus found
17		M.	Gastric ulcer		+		+	+		+	+	+	<1		12	Recovered	
18		F.	Gastric ulcer		+			+		+	+		5			Died (10th day)	Treated elsewhere for 8 days before readmission
19	M.		Normal stomach	+	+			o	o	+	o	+	2		11	Recovered	
20		F.	Gastric ulcer		+		+	+	o	+	+	o	<1		18	Recovered	
21	M.		Gastric ulcer		+	+	+	+	+	+	+	+	<1	7	23	Recovered	Abscess drained with suction

Table I.—DAMAGE TO UPPER ŒSOPHAGUS FOLLOWING ENDOSCOPY—*continued*

Table I.—Damage to Upper Œsophagus following Endoscopy—*continued*

Case No.	Under 50	Over 50	Diagnosis	Dysphagia	Pyrexia	Signs in Neck: Swelling	Signs in Neck: Supraclavicular Tenderness	Signs in Neck: Crepitus	Signs in Neck: Sterno-mastoid Spasm	X-ray Signs: Gas	X-ray Signs: Broadening	X-ray Signs: Osteophytes	Days to Onset of Treatment	Days to Operation	Days to Recovery	Result	Remarks
22		F.	Gastric ulcer		+	+	+	+		+	+	+	<1		13	Recovered	
23	F.		Gastric ulcer		+	+	+	0		+	+	0	1		9	Recovered	
Œsophagoscopy:—																	
24		F.	Œsophageal diverticulum		+		+	0		+	+	0	<1	4	19	Recovered	Abscess drained. Later further incision required
25		M.	Achalasia	+	+	0	+	0		+		+	1		13	Recovered	
26		F.	Atrophic gastritis		+		+	+	0	+	+	+	<1		6	Recovered	(Gastroscopy also performed)
27		F.	Hiatus hernia post-operative		+			0	0	+	0	+	1		9	Recovered	
28		M.	Normal œsophagus		+	+		+		+	+		<1	2	26	Recovered	Abscess drained with suction
29		F.	Hiatus hernia				+	+		+	+	+	<1		6	Recovered	

no X-ray film is available. This most important predisposing factor is present in *over* 75 *per cent* of cases.

If cervical osteo-arthritis is suspected a lateral radiograph of the neck prior to endoscopy is advisable to exclude a bony spur. *Fig.* 476 shows the unexpected osteophytes present in a healthy man aged 45 (*Case* 21); it also shows well the gas in the tissues and the broadening of the retrotracheal space. *Fig.* 477 shows the abnormal bony formation in *Case* 26 which probably accounted for the œsophageal damage in this instance.

Age and Sex Incidence.—Twenty of the cases were women, and 9 men. As approximately twice as many men as women are gastroscoped in this unit, women appear to be four times more prone to this injury. The incidence in women over 50 is far higher than in any other group. It is twelve times that of men under 50 (*Table III*).

This preponderance may be in part accounted for by the relatively high incidence of both atrophic gastritis (Swynnerton and Tanner, 1954) and of cervical osteo-arthritis in the over-50 age group, but does not account for the sex difference. Both Taylor (1945) and Fletcher and Jones (1945) quote cases in which a simple mucosal abrasion in an elderly woman caused a mediastinitis. Avery Jones recommends the use of the Wolff Schindler gastroscope in all women over 50, as he found that the majority of lesions were associated with the use of the Hermon Taylor instrument. The latter, though more satisfactory for examination of the stomach, particularly of the upper lesser curve, which is a not uncommon site for gastric ulcer, especially in women (Swynnerton and Tanner, 1953), has a longer rigid portion with a greater diameter and is therefore relatively more dangerous.

Skill of Examiner.—Though the majority of endoscopies are performed by the consultant staff (approximately 80 per cent) peri-œsophagitis occurred more commonly in cases examined by registrars. Lack of skill and experience is an important factor in the causation of these lesions. The only permitted movements of the rigid part of the instrument are axial rotation and longitudinal sliding (advance or withdrawal); any necessary antero-posterior or lateral deviation may only be brought about by readjustment of the patient's head. Adequate lubrication and gentleness in introduction are also essential.

Duration of Examination.—The few minutes required by the expert for the average complete examination may be increased three or four fold if one or two trainee gastroscopists also examine the case. If, as some believe (Barrett, 1952), the lesion is often due to a pressure necrosis of the œsophageal mucosa, this additional time may contribute to the risk.

Difficulty during Endoscopy.—Out of 29 cases, difficulty in instrumentation was recorded in only 1 case, where kyphosis prevented a complete gastroscopic examination. Difficulty due to kyphosis or lack of co-operation is encountered about once in every fifty gastroscopies, thus there is no significantly higher incidence of œsophageal damage in difficult cases; this is probably due to care in selection of subjects, and in readiness to abandon the examination

if undue difficulty is encountered. Clinical examination of the configuration and mobility of the cervicodorsal spine should always precede endoscopy. If severe, kyphosis or kyphoscoliosis may render endoscopy impossible, as may a severe deformity or

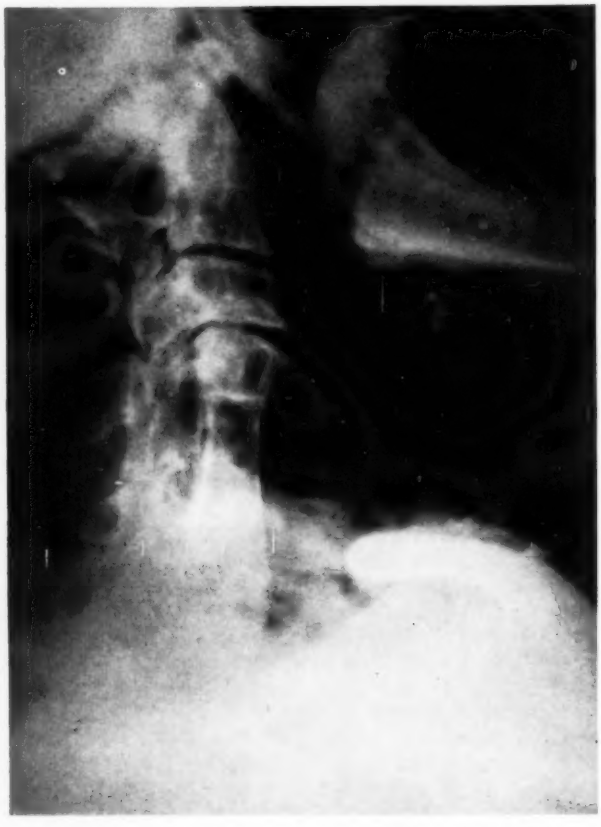

FIG. 477.—Bony abnormality with lipping of the cervical vertebræ, the probable cause of œsophageal damage at gastroscopy in a woman aged 61.

rigidity of the mouth or jaws. Even a full set of teeth may be a relative contra-indication.

Gastroscopy is best avoided, if possible, in the presence of certain conditions such as coronary disease, dyspnœa from any cause, chorea, epilepsy,

Table II.—RELATION OF GASTROSCOPIC DIAGNOSIS TO INJURY

	Percentage of Total Gastroscopies	*Percentage of Cases of Œsophageal Injury*
Normal stomach	34	38 (9 cases)
Gastric ulcer	35	29 (7 cases)
Gastric atrophy	5	33 (8 cases)
Other lesions	26	nil

paralysis agitans, and certain psychoses, also in an unco-operative and nervous patient. If essential in such cases, a general anæsthetic is often preferable to a local one. The majority of gastroscopies are performed under local anæsthesia, but the incidence of complications is no higher in those who have a general anæsthetic.

Diagnosis.—

Temperature.—This was elevated in every case, usually between 99° F. and 101° F.

Tenderness in the Neck.—Tenderness, particularly in the supraclavicular fossæ, was present in most cases. It was noted in 16 cases and was probably present unrecorded in many others. Supraclavicular tenderness was present in every case in which it was specifically looked for. In 3 it was observed before there was any evidence of surgical emphysema,

Table III.—ŒSOPHAGEAL INJURY RATE IN DIFFERENT AGE GROUPS

	Percentage of Total Gastroscopies	*Percentage of Cases of Œsophageal Injury*
Men under 50	30	7 (2 cases)
over 50	36	24 (7 cases)
Women under 50	14	14 (4 cases)
over 50	20	55 (16 cases)

which may be delayed many hours if the lesion is an abrasion or pressure necrosis as opposed to a frank tear.

Some degree of transitory dysphagia, soreness, or tenderness is frequently felt after gastroscopy, but usually higher in the neck. A series of 100 was observed from this aspect in the immediate

Table IV.—SYMPTOMS IN THE IMMEDIATE POST-GASTROSCOPY PERIOD (UP TO FOUR HOURS) IN 100 CASES

			Cases
Sore and/or tender at or above cricoid level			61
Sore and/or tender in suprasternal notch			4
Tender in one or both supraclavicular fossæ			2*
Other complaints, probably drug effects :	Nausea or vomiting	4	9
	Dizziness	3	
	Headache	2	
No complaints			26

* One of these two developed surgical emphysema on the following day (*Case* 17, *Table I*).

post-gastroscopy period: 61 were found to have some degree of discomfort at or above cricoid level (i.e., in the hypopharyngeal or pharyngeal region). A further 6 complained of soreness or tenderness low in the neck, but in only 2 was tenderness localized to the supraclavicular fossa. The only case of proved œsophageal damage in the series was one of these two (*Table IV*). It would appear that supraclavicular tenderness is frequently an early and reliable sign of peri-œsophagitis.

Clinical *swelling of the neck* may develop, but is not an early feature. Broadening of the retrotracheal tissues due to œdema, gas, or a collection of fluid, seen on lateral radiography is characteristic, and is present in almost every case.

Sternomastoid spasm is not a constant sign. It may be present at one time and absent a few hours later. It was noted as present in 4 of the cases and as absent in 5 cases.

Gas in the tissues of the neck is, of course, proof of damage to the œsophagus, whether it be a rapid widespread surgical emphysema suggesting a frank tear, or slower and more localized due to a minute hole or to a bruised mucosa resulting in either a slow perforation (Phillips, 1938) or invasion by a gas-producing organism.

The presence of gas is obvious in many cases as *crepitus*, but this is an unreliable sign and was absent in no less than 10 cases in which gas was demonstrated in the tissues by X-ray examination. Lateral radiography of the neck should be carried out at once in any suspected case.

Treatment.—Twenty-six cases were treated promptly, with no death, and low morbidity. Conservative measures were commenced at the first

suspicion of peri-œsophagitis, in all except one within 72 hours—namely, forbidding all food and fluid by mouth, and administration of intravenous fluids and full doses of penicillin.

Three cases did not come under the care of this unit for a week or more, by which time a fully developed mediastinitis was present. Two died; the third recovered slowly after drainage.

Of the 26 cases treated from the outset, 12 commenced treatment *within twenty-four hours* of endoscopy, only 3 (25 per cent) of these 12 were drained, and the average time to complete recovery was *fourteen days* (*Fig.* 478). Thirteen commenced treatment between twenty-four and seventy-two hours, 4 (31 per cent) were drained, average recovery time was nineteen days. One case showed no evidence of peri-œsophagitis till the fourth day, when a little dysphagia developed; radiography showed no gas till the seventh day; prompt treatment, with drainage, was carried out; recovery took twenty-eight days. In the cases drained the interval between endoscopy and exploration varied between two and twenty days, and did not appear to affect the interval between exploration and final recovery.

The histories of the three cases in which treatment was delayed for a week or more are summarized :—

Case 1.—A woman, aged 59, returned home on the day of gastroscopy. Sore throat persisted. She was not seen again till the seventh day when she was readmitted with developed mediastinal abscess which was drained through the neck. On the ninth day gastrostomy was performed. She deteriorated and died on the seventeenth day. Autopsy showed mucosal damage to the upper œsophagus, with mediastinitis and peritonitis.

Case 6.—A woman, aged 42, returned home on the day of gastroscopy. Sore throat persisted, treated as œsophagitis by her doctor for nine days. She was then readmitted with a mediastinal abscess which was drained, with recovery after thirty-three days.

Case 18.—A woman, aged 62, was treated elsewhere for eight days. On the fifth day an œsophageal lesion was suspected and penicillin given, but fluids by mouth were permitted. On readmission on the eighth day she had a severe mediastinitis and a pleural effusion. She rapidly deteriorated and died on the tenth day. At autopsy there was a 'pressure necrosis' of the hypopharyngeal wall, mediastinitis, and a septic pneumonia presumed to be due to inhalation of pus from a high rupture of a mediastinal abscess.

DISCUSSION

It is absolutely essential to institute conservative treatment directly the presence of dysphagia, pyrexia, or supraclavicular tenderness leads to a suspicion of œsophageal damage, without awaiting crepitus or radiographic proof of air in the tissues.

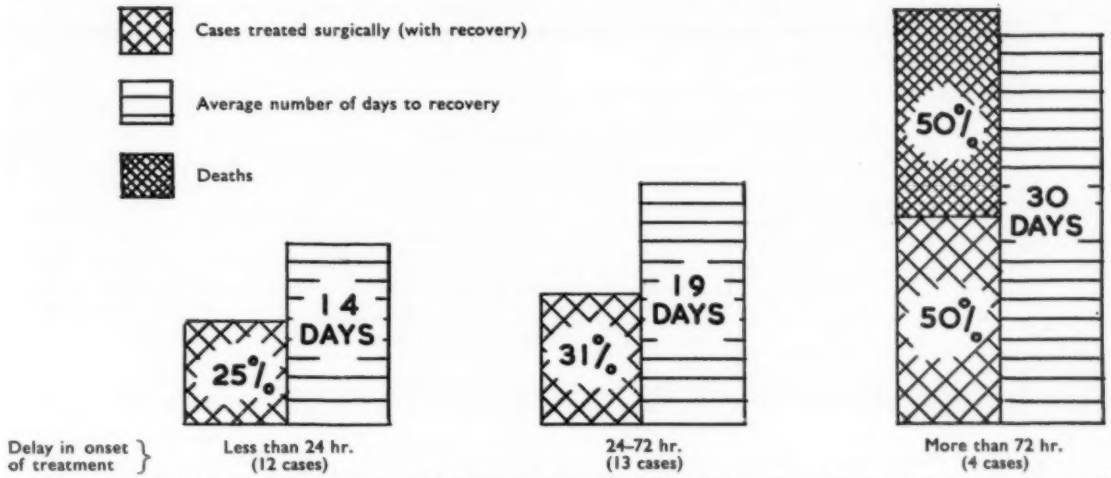

Fig. 478.—Relation of delay in onset of treatment to results. This diagram shows the dramatic increase in mortality and morbidity if treatment is delayed.

Nothing whatever is taken by mouth, even the swallowing of saliva is minimized by encouraging the patient to use a sputum mug. Fluids should be administered intravenously (or rectally as a temporary measure). Penicillin in full dosage is given.

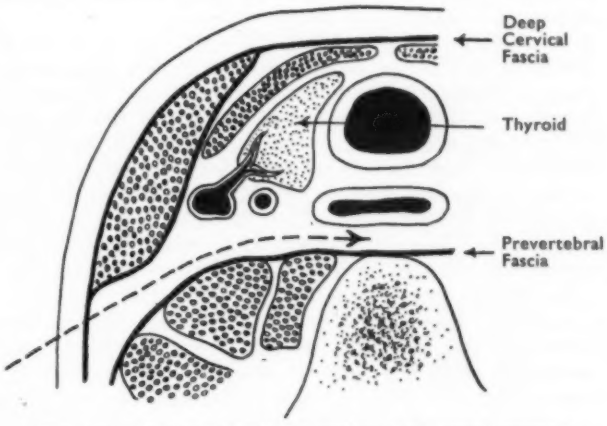

FIG. 479.—Section through the neck to show lateral approach to the retro-œsophageal space.

If these measures are applied early, and continued if necessary for several days until all signs of peri-œsophagitis have disappeared, recovery frequently occurs without the necessity for surgical intervention.

Early detection of œsophageal damage is of the utmost importance in forestalling a severe peri-œsophagitis, and the danger that a developing infection may be treated as a simple œsophagitis, a cervical

adenitis, or a chest infection, by the unwary is very real. Evidence of hypopharyngeal damage, either crepitus or tenderness in the supraclavicular fossa, was seen within forty-eight hours of endoscopy in 22 out of the 29 cases; in 11 of them within twelve hours. Every patient should be observed if possible for twenty-four hours after endoscopy and these signs particularly looked for. They should report at once any persistent sore throat or dysphagia.

The result of damage is at first a non-suppurative cervical peri-œsophagitis which may frequently be rapidly subside with no proof of damage (abou 1 per cent of endoscopies).

Prompt expectant treatment therefore in the firs instance will prevent many unnecessary operations The survival rate cannot be improved by early opera tion: it can be seen from our series that there were n deaths amongst those treated promptly by conserva tive measures. The treatment is continued unti signs of peri-œsophageal infection have disappeared

If increasing pyrexia, toxæmia, dysphagia, swel ling, and tenderness occur, operative measures mus

Table V.—Perforation of Lower Œsophagus due to Endoscopy. (All patients were over 50)

Case No.	Sex	Diagnosis	Result	Case Notes
Gastroscopy:— 1	M.	Carcinoma cardia	Died	At gastroscopy instrument appeared to enter peritoneal cavity. Epigastric tenderness present, and liver dullness absent, otherwise no signs of peritonitis. Emergency total radical gastrectomy performed. Specimen showed perforation at upper end of growth at cardia. Patient died a few hours after operation
2	F.	Duodenal ulcer	Died	At gastroscopy mid-œsophageal arrest occurred; instrument at once withdrawn with some hæmorrhage. Immediate severe pain in back and epigastrium. No dysphagia. Rapid onset of dyspnœa and extensive surgical emphysema. Repeated chest aspiration during next few days produced many ounces of turbid fluid. On tenth day a mediastinal abscess was drained by neck incision. Condition deteriorated with increasing dyspnœa and death two days later. Autopsy showed empyema and bronchopneumonia, a right subphrenic abscess, and a large tear in the posterior wall of the œsophagus at the level of the hiatus
Œsophagoscopy:— 3	F.	Carcinoma œsophagus	Died	Following œsophagoscopy the patient coughed every time she swallowed. Barium swallow showed barium in the mediastinum. She deteriorated and died ten days after endoscopy
4	F.	Hiatus hernia	Died	Aged 81. Slowly deteriorated and died 17 days after endoscopy, being diagnosed as bronchopneumonia. At autopsy a mediastinal abscess was found, adjacent to heart and right lower lobe, with acute purulent pericarditis
5	M.	Carcinoma cardia	Died	Following endoscopy complained of pain in right chest, diagnosed as lobar collapse. Radiography was negative. Slowly went downhill and died 13 days later. At autopsy a small perforation was found just proximal to a carcinoma of cardia, with an associated right empyema

aborted by prompt conservative treatment, though a minority of these cases may proceed to suppuration and require surgical drainage.

Goligher recommends immediate suture in every case of hypopharyngeal perforation as the only treatment offering a reasonable chance of survival. Jemerin (1948), reviewing 69 cases of œsophageal perforation, ascribes the marked fall in mortality in these cases since 1936 to operation (which he finds is now performed *early* in 90 per cent of cases instead of *later* in 50 per cent) rather than to the advent of antibiotics. Barrett (1952) also advocates immediate operation, though he allows expectant treatment in some cases, seen late, in which localization has occurred. He considers that antibiotics should not influence the decision to operate. He gives the mortality from perforation as nearly 50 per cent; which agrees with the figure collected from recorded cases in the literature, given earlier in this paper—a mortality of 35 out of 78 post-gastroscopy cases.

The advocates of early operation aim at closure of the perforation, but in many cases, probably the majority, there is no frank tear to repair; even the onset within a few hours of marked cervical crepitus is no proof that a macroscopic rent exists—many such cases subside without suppuration. In addition to cases where proof of œsophageal damage is forthcoming, there are a number of cases with symptoms following endoscopy sufficient to warrant institution of conservative treatment, and whose symptoms be employed. If in doubt a further lateral radiograph of the neck may show an increase rather than diminution in the retrotracheal swelling, or the presence of a fluid level may indicate abscess formation.

Primary suture is not applicable in these later stages as the presence of a spreading cellulitis or actual abscess cavity, with œdema and necrosis of the œsophageal tissues, will, as pointed out by Slesser (1951), render the œsophageal suture both difficult and unlikely to succeed. Instead, the retropharyngeal space in the neighbourhood of the lesion, which may be approached under local anæsthesia, can be drained with a gauze pack (Pearce, 1933) or with a rubber drain. If an actual abscess cavity is present, the latter method is preferable, using a small rubber tube placed down to the site of the damage, and applying continuous suction.

The usual approach medial to the sternomastoid and carotid sheath is necessary for the more extensive exposure required if suture is to be undertaken, but a simple alternative route for draining an abscess is through a small incision along the posterior border of sternomastoid just below cricoid level; once the deep cervical fascia has been broached, the exploring finger easily passes medially along the front of the prevertebral fascia; this plane leads directly to the retro-œsophageal space at the level where trauma usually occurs (*Fig.* 479). This route avoids penetrating the fascia between the thyroid gland and the carotid sheath in the region of the middle thyroid

vena. After sucking out the pus from the abscess cavity a rubber tube is passed along the track, the skin approximated around the tube, and continuous low-pressure suction applied.

If no œsophageal fistula is present fluids may be commenced by mouth in 24 to 48 hours and the suction continued till the flow of pus ceases. The tube is then shortened and finally withdrawn, probably within a week of the operation.

If an œsophageal fistula is present (readily demonstrated in a doubtful case by swallowing a mouthful of dilute methylene blue) the suction is continued until the fistula has closed (usually less than a fortnight), but fluids by mouth may be commenced after a few days, when the signs of inflammation have subsided. We have had no case in which the fistula persisted for more than three weeks, but should this occur it would be as well to shorten and eventually withdraw the tube, but keeping the track open until the fistula closes.

Late Effects.—The majority of cases of œsophageal damage subside without further trouble, but occasionally a stricture may result. This fibrous narrowing may rarely require bouginage. Occasionally a small œsophageal pouch remains at the site of the injury; two cases of false diverticulum of this nature are on record in this unit.

INJURY TO THE LOWER ŒSOPHAGUS

Perforation of the thoracic œsophagus due to endoscopy is uncommon, but is a serious and frequently fatal complication. It is often associated with a carcinoma.

Five cases have occurred in this unit, all fatal (*Table V*). Three were associated with carcinoma. One occurred in a frail old lady of 81 and was not diagnosed until autopsy. The fifth is an unusual case of gastroscopic perforation in the region of the œsophageal hiatus; though suspected at the time, the patient was treated by conservative measures, with belated cervical drainage of the mediastinal abscess which had extended upwards. It seems possible that this case, the only one of its kind we have encountered, might have been saved by prompt thoracotomy and repair of the perforation as advocated by Barrett (1952).

Diagnosis may be difficult in these cases and a respiratory infection may be suspected. In any case of doubt a lipiodol swallow under X-ray examination may clinch the diagnosis. Immediate suture, which is probably the treatment of choice in lower œsophageal perforations, is of course impracticable where the perforation is associated with a carcinoma. In such a case the possiblity of immediate resection should be considered.

PERFORATION OF THE STOMACH

Gastric perforation, as already pointed out, is a rare complication of modern gastroscopy. There has been no known case in this unit in a series of over 10,000 gastroscopies.

Conservative treatment is usually advocated; peritoneal contamination is usually minimal, as the stomach is usually clean and empty at the time, and laparotomy frequently fails to demonstrate any visible perforation. Recovery is usually uneventful if the stomach is kept empty for two or three days by continuous gastric aspiration, during which time fluid balance is maintained intravenously.

Perforation of the jejunum at gastroscopy should, on the other hand, be treated by laparotomy and suture.

SUMMARY

The complications of gastroscopy and œsophagoscopy are reviewed, the most frequent being trauma to the œsophagus in the post-cricoid region.

A case of osteomyelitis of the mandible following gastroscopy is recorded.

Twenty-nine cases of upper œsophageal damage are analysed, with discussion of causation, diagnosis, and treatment.

The importance of early diagnosis and treatment is stressed; conservative treatment is advocated in the first instance.

Five cases of endoscopic perforation of the thoracic œsophagus are presented.

CONCLUSION

The early recognition and treatment of complications will practically eliminate the mortality and morbidity; with due care in selection of cases and in the handling of the instrument, the majority of complications, particularly those due to gastroscopy, can be avoided and gastroscopy rendered, as Henning says, " no more dangerous than the passage of a soft stomach tube ".

We would like to thank Miss E. Mason for photo-radiographs and Mrs. J. Mace for *Figs.* 475 and 477; also Dr. B. F. Swynnerton for his help.

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ŒSOPHAGEAL STRICTURES ASSOCIATED WITH GASTRODUODENAL INTUBATION

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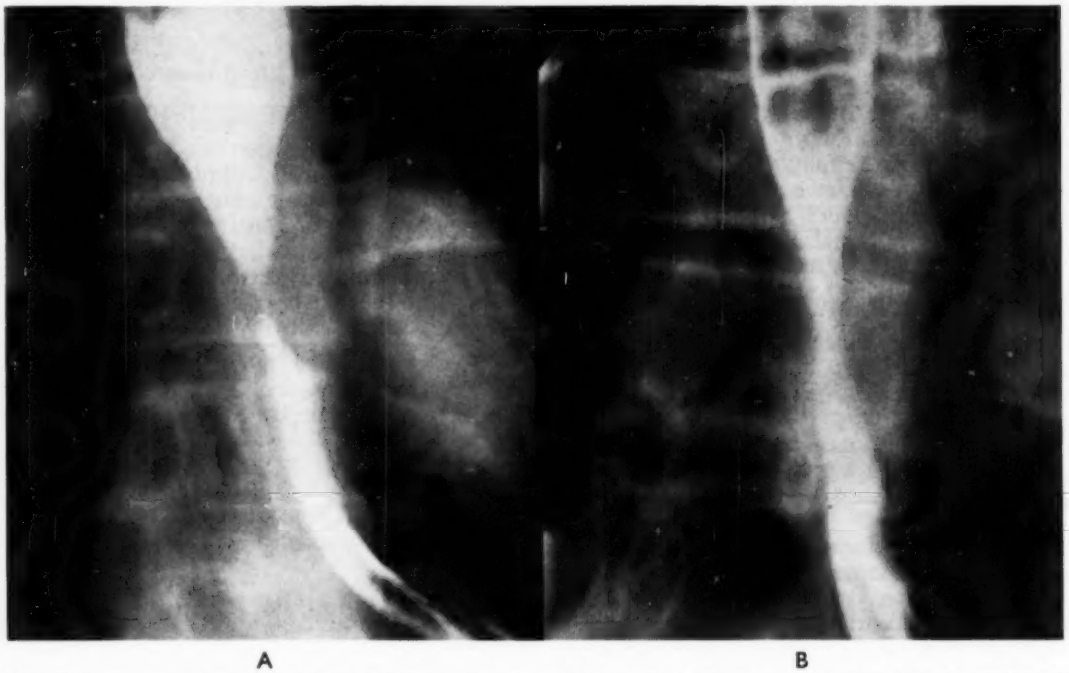
It has been recognized in the past that certain œsophageal strictures may occur without obvious cause. A number of these cases have been reported in the literature, and a study of them has elucidated certain facts which may have a bearing on the aetiology.

Firstly, in the majority of these cases the past history has disclosed the presence of an abdominal lesion, mainly gastroduodenal, for which generally an operation has been carried out and in the course of treatment a gastroduodenal tube, such as a Ryle's tube, has been passed for a varying length of time. Secondly, the symptom of dysphagia has arisen at a varying interval after the removal of the tube, and at a later date as a result of radiological and endoscopic investigation an œsophageal stricture has been found. Thirdly, the stricture generally arises in the same part of the œsophagus—namely, in the lower one-third. Fourthly, prior to the insertion of the tube vomiting has been at one stage of the patient's clinical history a prominent symptom.

This paper reports 5 cases which have been seen in this hospital and which appear to fall into this category.

CASE REPORTS

Case 1.—Male, aged 52, admitted in September, 1948, with a perforated duodenal ulcer. A Ryle's tube was passed and an immediate toilet and suture of the perforation was carried out. After the third day the tube was removed, and on the sixth day he noted a sense of roughness at the back of his throat. This was particularly noticeable on eating crust. He was discharged on Sept. 22, but these symptoms persisted. On Nov. 1, he attended the out-patients department stating that he now had definite difficulty in swallowing and occasionally regurgitated his food. He also complained of epigastric pain occurring one to two hours after food, and a barium meal revealed the presence of a prepyloric ulcer. This was considered to be the cause of his symptoms and conservative treatment was advised. His symptoms settled on this régime. Six months later he attended again, complaining of dysphagia with regurgitation of food. A barium swallow was done (*Fig.* 480 A) and this showed a smooth constriction at the lower end of the œsophagus. The wall of the œsophagus appeared thickened above the stricture, which suggested the presence of muscle spasm. A provisional diagnosis of cardiospasm was made and the inhalation of octyl nitrite tried, but without producing any material relief. Meanwhile his epigastric pain recurred, and so in May, 1950, he was re-admitted for investigation. This time he was seen by Mr. Frank Nicholson, who did an œsophagoscopy and reported that there was no dilation of the œsophagus or œsophagitis. There was no evidence of a stricture and nothing to indicate either a carcinoma or cardiospasm. On July 12, the barium swallow was repeated (*Fig.* 480 B); it showed a smooth constriction of the lower end of the œsophagus, several inches in length. There was no evidence of hiatus hernia. After the œsophagoscopy his swallowing improved somewhat. Later, however, his dysphagia worsened and he had to be re-admitted on Aug. 31 for another œsophagoscopy and dilatation. This



A B

FIG. 480.—*Case* 1. A, Barium swallow showing a smooth constriction at the lower end of the œsophagus. At this stage the diagnosis made was cardiospasm. Œsophagoscopy revealed no stricture. B, Barium swallow repeated two years later. The constriction at the lower end of the œsophagus had persisted. Therefore benign fibrous stricture strongly suggestive.

tir e the cardia was reached at 41 cm. and was seen to be ur formly narrowed, only admitting a size 10 English bc igie. It was dilated easily to size 18. The appearances in icated cardiospasm. A biopsy taken at the time sh wed only normal squamous epithelium (*Fig.* 481). Af er this, his swallowing once more improved and the pa ient was again advised inhalations of octyl nitrite in an attempt to overcome the spasm. No relief was

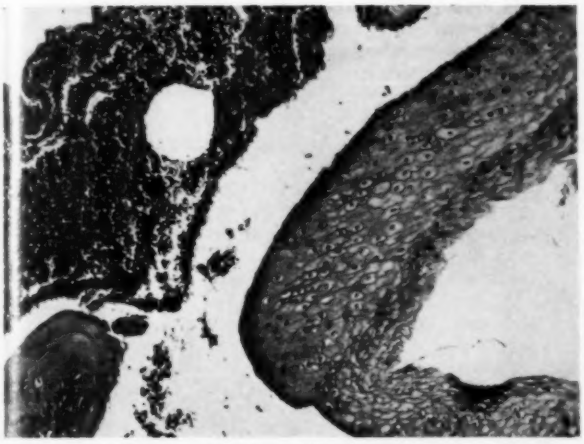


FIG. 481.—*Case* 1. Histology slide shows normal squamous epithelium. No sign of inflammation. (× 67.)

produced and on Sept. 1 he was œsophagoscoped. Again the œsophagus was seen to be narrowed in the region of the cardia. A biopsy taken at the time showed the presence of granulation tissue (*Fig.* 482). The narrowing was this time considered to be due to stricture rather than to cardiospasm.

He continued to attend at intervals for œsophagoscopy and dilatation. On March 17, 1953, he was re-admitted with a perforated anastomotic ulcer. A Ryle's tube was passed and the perforation was repaired by a toilet and suture, combined with a vagotomy. He made a successful recovery and was discharged home on March 31.

On Feb. 25, 1954, he was admitted with complete dysphagia to solid food, but was able to swallow liquids fairly well. The stricture was dilated to the size of a number 20 bougie. Since then, dilatation has not been necessary.

Case 2.—A male, aged 60, was first admitted to the Manchester Royal Infirmary, under the care of Mr. R. L. Newell, in November, 1950, with a perforated duodenal ulcer. A Ryle's tube was passed and the patient was operated on, when a toilet and suture of the perforation was done. The following day the Ryle's tube was removed. He made an uninterrupted recovery, apart from one episode of vomiting. He was discharged after fourteen days. When seen about a fortnight later in the out-patient department, he complained of having had frequent episodes of vomiting associated with epigastric pain. He had that morning vomited two pints of fluid. He looked ill and dehydrated, and he was admitted forthwith as an emergency. Pyloric stenosis was diagnosed, and initially he was treated conservatively with daily gastric lavage and an intravenous drip of glucose-saline. After a week of this treatment a gastro-enterostomy was done and a Ryle's tube, previously passed, was maintained for several days. The patient's condition improved considerably thereafter, and he was finally discharged after six weeks in hospital. In October, 1951, he first complained of dysphagia. He stated that the food would stick at the lower end of the œsophagus initially, but would eventually pass on, especially if helped on by liquids. It was thought at first that his symptoms were functional and he was discharged with instructions to attend later. He re-attended in January, 1952, and by now his dysphagia was much more severe. A barium swallow was done (*Fig.* 483), which showed that the barium passed readily down the œsophagus to a point 2 in. above the level of the diaphragm, where there was a constantly narrowed area, associated with one or two ulcer craters. The appearances suggested a benign stricture, and at œsophagoscopy by Mr. Frank Nicholson definite

FIG. 482.—*Case* 1. Histology slide shows granulation tissue. Presence of inflammatory changes in the œsophagus confirmed at a late stage. (× 30.)

FIG. 483.—*Case* 2. Barium swallow reveals an undoubted stricture, corresponding to œsophagoscopy findings, at the lower end of the œsophagus.

œsophagitis was seen at 37 cm., but no sign of an underlying ulcer. Below this region a stricture was seen which was dilated to the size 17 English œsophageal bougie. A week later the œsophagoscopy was repeated and this time the stricture was easily dilated to a size 24 bougie. His swallowing improved considerably after this, but by July, 1952, it had again become difficult, so that dilatation of the stricture had to be repeated. Since then the patient has been symptomless.

Case 3.—A male, aged 61 years, was admitted to Rochdale Infirmary in October, 1951, with a perforated duodenal ulcer. A Ryle's tube was inserted and the perforation was repaired surgically. The Ryle's tube was removed after three days. He made an uninterrupted recovery, but early in December, 1951, he was re-admitted because of recurrence of his ulcer symptoms, and a partial gastrectomy was carried out. A Ryle's tube was again passed and maintained in situ for seven days. He was in hospital altogether for twenty-one days, and after he had been home a week he first noticed difficulty in swallowing solid food. He felt the food stick at the lower end of the sternum and the discomfort could only be relieved by regurgitation of the food. The dysphagia increased in severity until he was only able to take liquids. At this stage he was re-admitted to Rochdale Infirmary in January, 1953. An œsophagoscopy was done by Mr. Vernon Smith, who found a stricture at the lower end of the œsophagus. A biopsy was taken and the histological report read : " The material is fragmentary, but there are several clumps of neoplastic cells, which are probably part of an anaplastic epithelioma ".

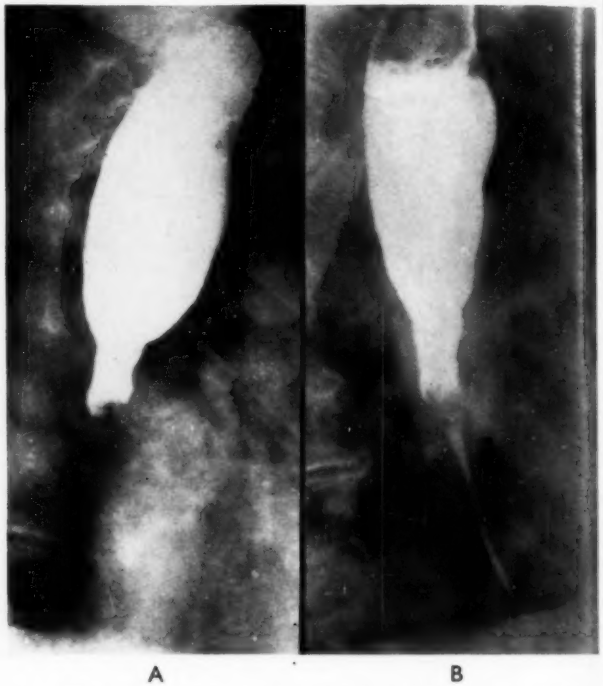
Therefore, the patient was referred to the department of thoracic surgery at the Manchester Royal Infirmary. He was seen by Mr. Graham Bryce, who advised that the patient be admitted for an exploratory operation. A barium swallow (*Fig.* 484 A) had previously shown an apparent delay at the lower end of the œsophagus, but no irregularity of outline. At operation the œsophagus was found to be entirely free of any neoplastic or other lesion. The patient made an uneventful recovery. However, there was still some evidence of œsophageal obstruction. By the time of his discharge from hospital, he was able to pass a No. 16 English bougie. He was sent home with a size 14 bougie with instructions to carry out self-bouginage twice a week. His swallowing remained satisfactory for four months, but by then his swallowing had become more difficult. He was again re-admitted for œsophagoscopy and bouginage. Another barium swallow was done (*Fig.* 484 B), which confirmed the presence of a smooth tapering defect in the lower third of the œsophagus. His condition has remained satisfactory since.

Case 4.—A male, aged 66, was admitted to Withington Hospital in June, 1951, with symptoms suggestive of uræmia. A Ryle's tube was passed and maintained in situ for two weeks. Immediately after removal of the tube he experienced nausea and chest pains accompanied by coughing and the expectoration of thick mucous. He also had revulsion to food in general and occasionally a total inability to swallow meat. In March, 1952, he was referred to the Manchester Royal Infirmary, because of increasing difficulty in swallowing. A barium swallow revealed no abnormality, but as time went on the swallowing became increasingly difficult. In October, 1952, the barium swallow was repeated and this time it showed a smooth persistent narrowing in the lower third of the œsophagus. An œsophagoscopy was done by Mr. Frank Nicholson. At 35 cm. a narrowing of the œsophagus was seen, associated with localized œsophagitis. The narrowed segment easily took a No. 14 English bougie. Eventually the œsophagoscope, an adult Negus type, slipped into the stomach. His swallowing improved considerably thereafter, but eight months later the stricture was again dilated. Since then his swallowing has been reasonable, but he still experiences feelings of discomfort.

Case 5.—A male, aged 53 years, was admitted to the Manchester Royal Infirmary under the care of Mr. H. T. Simmons, in May, 1953, with a carcinoma of the rectum, for which an abdominoperineal resection was carried out. Five days after the operation it was suspected that paralytic ileus had developed. A Ryle's tube was passed

A B

FIG. 484.—*Case* 3. A, Barium swallow shows a smooth tapering defect at the lower end of the œsophagus. Presence of a fibrous stricture was not confirmed at this stage. B, Barium swallow shows an irregularity of outline, suggesting a fibrous stricture at the lower end of the œsophagus. This was confirmed on œsophagoscopy.



A B

FIG. 485.—*Case* 5. A, Barium swallow shows a complete obstruction at the junction of the middle and lower thirds of the œsophagus. This was caused by a bolus of food. Removal of this at œsophagoscopy was carried out, but a stricture was seen. B, Barium swallow, repeated at a later date, shows the presence of a stricture at the junction of the middle and lower thirds of the œsophagus.

nd an intravenous saline drip set up. After a further ive days the Ryle's tube was removed and the patient ontinued to recover. On the thirty-seventh day he was lischarged home, but in September, 1953, he attended he out-patient department complaining of regurgitation of food, which occurred on occasions only. No action vas taken at the time, and when he attended the following nonth he had put on 2 st. in weight and stated that he vas very well. In February, 1954, he was admitted to he Manchester Royal Infirmary in a state of acute lehydration. He gave a history of having vomited ontinuously for the previous five days. He stated that ie had had twelve similar attacks in the last three months, ach lasting two days. On admission a Ryle's tube was assed and an intravenous saline drip was set up. After even days the patient's condition had improved and by his time the tube had been removed. When his general ondition had improved sufficiently, a barium swallow vas done (*Fig.* 485 A). This showed narrowing of the umen of the œsophagus at the junction of the middle and ower one-third. The patient was then œsophagoscoped, sing a medium-sized Negus type. The instrument assed to 33 cm. and at this point a stricture was found. The mucous membrane bled freely on being touched with the sucker. There appeared to be a friable growth presenting on the (right) lateral wall. Biopsy (*Fig.* 486), however, showed the specimen to consist of granulation tissue heavily infiltrated with lymphocytes, plasma-cells, and polymorphs. There was no evidence of malignancy. The stricture was dilated to size 7 bougie. After this œsophagoscopy the patient's swallowing improved, but when at a later date the barium swallow was repeated a stricture was still seen to be present (*Fig.* 485 B). No further dilatation has as yet been necessary.

DISCUSSION

In all, about 23 similar cases have been reported in the literature since 1915, when McKinney published an account of this condition and discussed the aetiology, with particular regard to the importance of the regurgitation of gastroduodenal contents as a factor in the production of these strictures.

The chief problem to be discussed is the extent to which the gastroduodenal tube is concerned with the production of these strictures.

Gerhard Straus (1925) states that these strictures could be caused by the trauma of the passage and presence of such a tube, producing thrombosis of intramural veins and resulting in fibrosis of the œsophageal wall. Kegaries (1934) carried out some work on the anatomy of the veins draining the œsophagus, and emphasized the presence of a complex venous anastomosis. He considered that trauma may play some part in the production of rupture of submucous veins, but not by a Ryle's tube. A larger tube might produce this effect.

The presence of a Ryle's tube has been a constant feature in all our cases; and these strictures have developed at a varying interval after the passage of the tube (*Table I*).

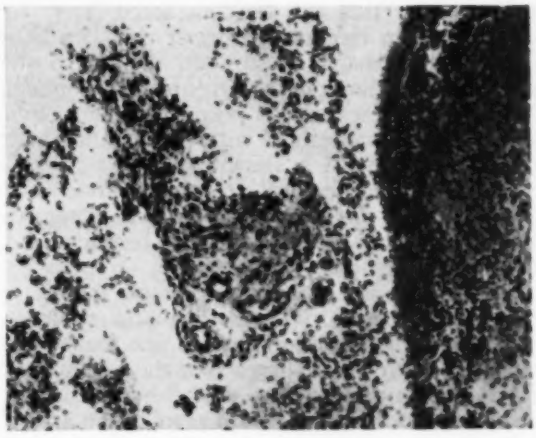


FIG. 486.—*Case* 5. Histology slide showing granulation tissue. (× 112.)

It will be seen that there is no constant relationship. In most, a Ryle's tube has been passed more than once, and on each occasion for periods which have varied from one day to two weeks. Once the Ryle's tube has been finally removed there has sometimes been an appreciable delay before the first symptom has been noticed. There is no constant time interval between the length of time the Ryle's tube has remained in situ and the interval before the first symptom has been noticed. One may gather from a study of the table that the Ryle's tube may play, at best, only an incidental part in the production of an œsophageal stricture. It is in any case, logical to think that even if trauma does play a part, once the cause of the trauma has been removed the lesion might eventually heal fairly quickly without necessarily resulting in permanent damage.

In *Case* 1 the Ryle's tube was in position for three days. Three days later the patient noticed a sense of roughness at the back of the throat. Yet seven months later a stricture was recognized, which persists to this day. In *Case* 2 and 4, where the tube remained in situ for two weeks continuously,

Table I.—RELATION OF PASSAGE OF RYLE'S TUBE TO APPEARANCE OF ŒSOPHAGEAL STRICTURE

	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5
Number of times tube passed	1	2	2	1	1
Duration	3 d.	1 d.—1st time 14 d.—2nd time	3 d.—1st time 7 d.—2nd time	14 d.	5 d.
After removal of tube, appearance of first symptom	3 d.	10 mth.	4 wk.	Next day	4 mth.
Nature of first symptom	Sense of roughness in throat	Dysphagia	Dysphagia	Dysphagia	Dysphagia
Recognition of stricture, after removal of Ryle's tube	7 mth.	12 mth.	2 yr.	16 mth.	9 mth.

one might possibly think that permanent damage would result.

Except in *Case* 5, all the other strictures are noted to have occurred in the lower third of the œsophagus. This is borne out by a study of other reported cases. The reason for this will be considered later. The initial change in the œsophagus at this site is very often an hæmorrhagic erosion on the left postero-lateral wall, associated with surrounding œsophagitis. In other cases œsophagitis occurs without obvious ulceration. In association with these inflammatory changes, screening has shown that muscle spasm may be a marked feature. *Case* 1 illustrates this. When, at a later date, radiology and œsophagoscopy reveal a persistent stricture, fibrosis has occurred in the muscle layers.

Certain authorities have suggested that it may have resulted from persistent muscle spasm. A knowledge of the pathology makes one realize that a time lag between the occurrence of the first symptom and the recognition of an established stricture is understandable, but this would seem to be a further reason why the initial œsophagitis, with or without superficial ulceration, should quickly heal were the Ryle's tube to be the major cause.

There must be other, and perhaps more important, factors concerned. These will be considered in the order of the least important first.

1. The Relationship between Upper Abdominal Lesions and Œsophageal Strictures.—Gerhard Straus (1925) says that œsophageal strictures may be due to the presence of such lesions as cholecystitis and duodenal ulceration, resulting in a thrombophlebitis of the gastric veins which has spread in a retrograde fashion to the lower œsophageal venous plexus and resulted, in his opinion, in fibrosis of the œsophageal wall. This may be a possible reason why these strictures are commonly located in the lower third of the œsophagus. Elmer C. Bartels (1935) in his exhaustive study of 85 cases of œsophagitis, on a microscopical study of many specimens has not been able to demonstrate evidence of venous thrombosis. Further, it would seem that if this were so important a factor, then these strictures should be much more common. The degree of infection in many cases of duodenal and gastric ulceration is small, and it seems difficult to understand why thrombophlebitis, let alone retrograde thrombophlebitis, should occur. Finally the presence of an upper abdominal lesion is by no means constant in these cases. *Case* 4 demonstrates this. The predominant feature in this case was the uræmia of renal origin.

2. Vagotomy.—In *Case* 1, following the perforation of an anastomotic ulcer, a vagotomy was carried out. Gerhard Straus had one case following vagotomy. He attributed the production of an œsophageal stricture to the trauma caused to the tissues. Following the vagotomy he applied silver clips to the cut ends of the nerves. The stricture occurred exactly in between these clips. Dysphagia commenced on the tenth post-operative day. This could be an additional reason for these strictures occurring generally in the lower third of the œsophagus.

It is stated that vagotomy predisposes to gastric atony and achalasia of the cardiac sphincter. However, Hwang, Essex, and Mann (1947), on the basis of work carried out on dogs, said that the vagus nerve contains both inhibitory and motor-fibres to the cardia. They found that the tone of the vagus was not increased after vagotomy. This is borne out by clinical observation. Dysphagia is not a common symptom after vagotomy, and indeed strictures rarely occur after this operation. Perhaps as Straus suggested, the only type would be in association with trauma to the wall of the œsophagus produced by severe manipulations, and particularly on the œsophagus during the isolation of the vagi.

3. Regurgitation of Gastroduodenal Juices.—In recent years great stress has been laid on the effect of regurgitation of gastric and duodenal juices on the œsophageal mucosa. If the sphincteric mechanism at the lower end of the œsophagus is deficient, then acid and pepsin may flow readily back into the œsophagus during sleep when the recumbent position is associated with muscular relaxation. The pool of gastric juice in the œsophagus may cause œsophagitis with ulceration, and later give way to fibrosis and stricture formation (Barrett, 1950). The reflux of gastric contents is normally prevented by the oblique entrance of the œsophagus into the stomach, the sphincteric action of the right crus, and, during inspiration, by the diaphragm shortening, so that the looping fibres of the constricting right crus pull the œsophagus down into the abdomen, so increasing the obliquity of the angle of the œsophagus with the stomach (Avery Jones, 1953).

There are many instances recorded where reflux of gastric contents has been seen to occur: Kirklin (1934) and his associates at the Mayo Clinic observed 150 cases. All these cases were well and ambulant; 15 per cent were observed to have regurgitation of gastric contents when placed in the recumbent and Trendelenburg position. Only 2 in. of the distal third of the œsophagus was filled however. If this is found in ambulant cases, the frequency in those acutely ill must be high.

Bartels (1935) emphasized the importance of regurgitation as a factor which may produce œsophagitis under certain conditions, and result in stricture formation.

Guisez (1923) stated that spasm, if prolonged, may produce stricture formation. In this he is supported by McKinney (1915), who found that fluoroscopy revealed spasm not seen at endoscopy. For spasm to occur, however, it is necessary that the cardia remains patent so that the regurgitated acid secretion may continue its corrosive effect on the diseased area. Robins and Jankelson (1926) observed 105 normal cases in which they were able to observe this taking place.

Friedenwald, Feldmann, and Zinn (1928) showed in experiments on dogs that prolonged retention of acid and pepsin in the mucosa of the œsophagus is harmful.

Prolonged post-operative vomiting is probably the factor which is most harmful, especially in association with a deficient circulation. Vomiting has been a common symptom in all 5 cases reported in this article. It would be difficult to assess how great a part this may have had to play in producing these strictures; the evidence seems overwhelming to support a claim that at any rate regurgitation of

cid gastric, and even alkaline duodenal juices, into he œsophagus continued over a period of time vill result in œsophagitis, which if severe enough vould cause fibrosis and stricture formation.

4. Debilitation.—This is not considered to be a najor factor in itself; but in association with others t may play a part. It has been noted that at a ertain point in each of these case histories the atient's general condition has been poor, as a result f the long-standing disease associated with frequent ttacks of vomiting. It has already been intimated hat if the blood-supply of the lower end of the esophagus becomes poor, as it would in seriously ll patients, then, whatever major primary factors are onsidered to be the cause of the production of these trictures, they will have a much more powerful ffect.

CONCLUSIONS

The weight of evidence would appear to be gainst regarding the Ryle's tube as the major actor producing these strictures. If this were so mportant, then the consequence of passing such a ube would have to be much more seriously considered. The type of patient in whom a Ryle's tube has to be passed is commonly one who is suffering from some gastro-intestinal condition causing pain and vomiting. The tube is passed either to relieve the vomiting or as an aid in the operative treatment of such lesions. That gastro-intestinal disease is not the only prodromal factor is well known. What, however, is common to all these cases is the symptom of vomiting, and the vomiting is generally prolonged and persistent. Therefore, one comes to the conclusion that the most important single factor in the production of these strictures is the effect of regurgitation of gastroduodenal juices into the lower third of the œsophagus. The presence of a gastroduodenal tube may act as an important secondary factor by disturbing the mechanism of the cardiac sphincter and perhaps by altering the œsophagogastric angle. If the patient is comparatively well and healthy, then neither of these factors may exert a permanent damaging effect. If, however, the patient is debilitated so that the blood-supply of the œsophagus is interfered with, then the combination of these three factors, regurgitation, the gastroduodenal tube, and debilitation, may result in a stricture being formed.

SUMMARY

Five cases of œsophageal stricture are reported. Four followed major upper abdominal disease; the fifth followed uræmia.

The important clinical and pathological features are considered.

Five aetiological factors are discussed. It is decided that the regurgitation of gastric and duodenal juices combined with the presence of a gastroduodenal tube in a debilitated patient would result in the formation in many cases of an œsophageal stricture in the lower third of the œsophagus.

My thanks are due firstly to Mr. Frank Nicholson for primarily suggesting this investigation, and also for his kindly criticism and encouragement during the preparation of this article. Secondly to Mr. Graham Bryce, Mr. Sutherland, Mr. Newell, and Mr. Simmons, for allowing me to publish their cases. Finally to Dr. Robert Ollerenshaw, Mr. Kilshaw, and members of the Medical Illustration Department of the Manchester Royal Infirmary, for producing the photographs.

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THE SIGNIFICANCE OF GASTRIC MUCOSA IN THE ŒSOPHAGUS

BY NORMAN WYNDHAM, SYDNEY

THIS paper is concerned mainly with questions of terminology and histology in the case of œsophageal stricture occurring in a child, the lower half of the œsophagus being lined by gastric and intestinal epithelium, and in whom there was no œsophageal hiatus hernia. Although the material was obtained from only one case, there are several features which are considered sufficiently important to make a contribution to the subject.

TERMINOLOGY

Barrett (1950, 1954) referred to cases of stricture of the œsophagus occurring well above the diaphragm. Below the stricture there was gastric mucosa lining what appeared to be œsophagus. In these cases, however, he claimed that the stomach was situated in the mediastinum and that the condition was, in reality, a stricture at the junction of a short œsophagus and a high stomach. The absence of peritoneum was

described as being due to an extension of the bare area of the stomach.

Allison and Johnstone (1953) described similar but not identical findings in 11 cases. In these the stricture was highly placed and situated at the junction of stratified squamous mucosa and columnar epithelium of gastric pattern, the latter lining a tube having all the appearance of being œsophagus and

Paul was a boy, aged 9 years, the youngest of three mal children, who was referred by Dr. G. McDonald, actin Honorary Consulting Physician at the Auburn Distric Hospital, Sydney. The child's mother stated that fro birth he had had difficulty in swallowing. Questioning o the mother after the final diagnosis has been made clea showed that the symptom was a true dysphagia and no regurgitation of food sometime after eating. His ability to swallow fluids improved until, by the age of 7, he wa

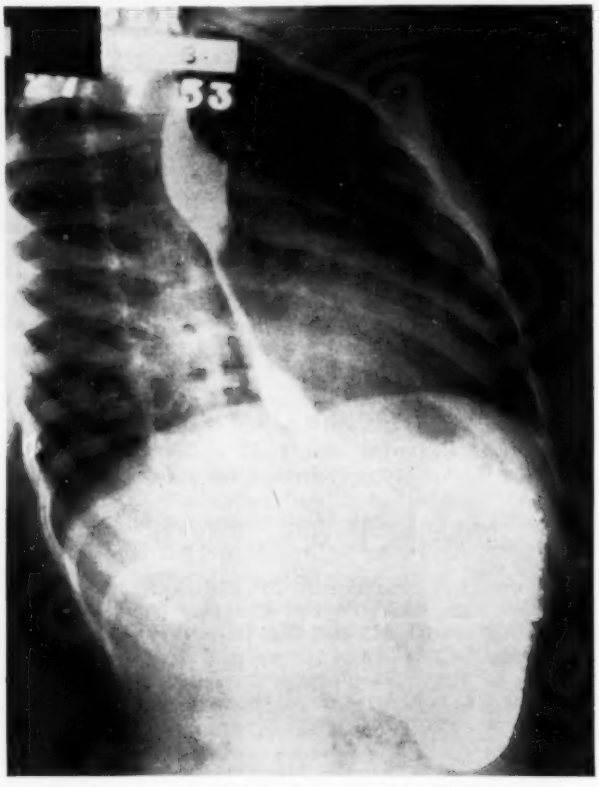

FIG. 487.—Showing stricture of œsophagus. The absence of hiatus hernia was confirmed at operation.

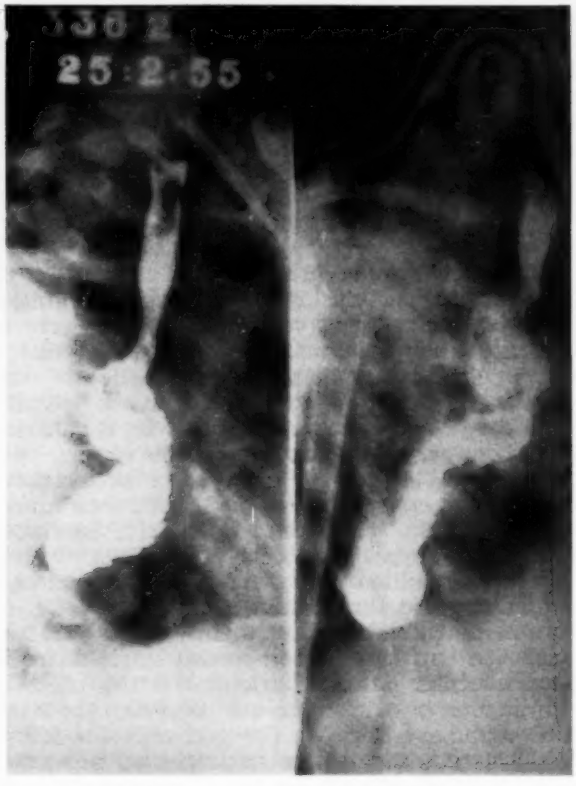

FIG. 488.—Nine months after jejuno-œsophagostomy.

joining, inferiorly, a herniated cardiac end of stomach. They speak therefore of an "œsophagus lined by gastric mucous membrane".

Findlay and Brown Kelly (1950) reported 9 cases of children with œsophageal stricture of which 7 were mid thoracic in position. In these the stomach was described as being drawn up into the chest to join a congenitally short œsophagus. The stricture occurred at the junction of the two. The tracings of the radiographs in these cases do indeed support this view.

It can be seen, therefore, that opinions differ even in the few papers quoted as to whether œsophagus should be identified by its epithelium or its gross structure. Further, in all cases of this kind so far found in the literature there has been an accompanying œsophageal hiatus hernia.

In the case to be reported here the œsophagus below the stricture was lined by epithelium which was not only of gastric pattern but also one possessing intestinal villi. Neither was there any evidence radiologically or by direct examination of hiatus hernia.

CASE REPORTS

Reference is made only to those features of the case considered pertinent to this discussion.

able to live on a diet of milk and ice-cream with only occasional regurgitation of food. When seen at the age of 9, he had never eaten meat. He was thin, pale, undersized, bright mentally and of a mischievous, happy disposition.

The child had been seen by doctors on several occasions in early childhood but the diagnosis had been missed although several X-ray examinations of the alimentary canal had been performed. These films were not available. At the age of 9 he was seen by Dr. McDonald because of increasing dysphagia.

X-ray examination (*Fig.* 487) showed a long narrowing of the œsophagus in its middle third, extending almost to the level of the aortic arch. At that time no specific examination was made of the efficiency of his œsophageal hiatus mechanism, but this was done subsequently and shown to be normal. This was later confirmed at operation. Probably because of this, the narrowing was thought by the radiologist to be a developmental abnormality. The writer shared this opinion.

Dilatation of the stricture was performed once by Mr. E. McA. Steel without difficulty, but was unsuccessful on all subsequent occasions. Excision of the stricture was therefore advised and was carried out on Oct. 22, 1953. To all external appearances the œsophagus passed normally into the abdomen, the cardio-œsophageal junction being well below the diaphragm, as can be seen in the

radiograph. There was no gastric herniation or patulousness of the œsophageal hiatus. The stomach could not be lifted into the thorax until the œsophageal hiatus had been stretched and the stomach mobilized. The mediastinal connective tissue around the œsophagus showed signs of inflammation, being œdematous and vascular and containing large, soft lymph-nodes. A stricture was found just below the aortic arch. It was annular and only 3 cm. long. The œsophagus above and below it appeared to be normal. The stricture and lower part of the œsophagus was excised and a gastro-œsophagostomy performed.

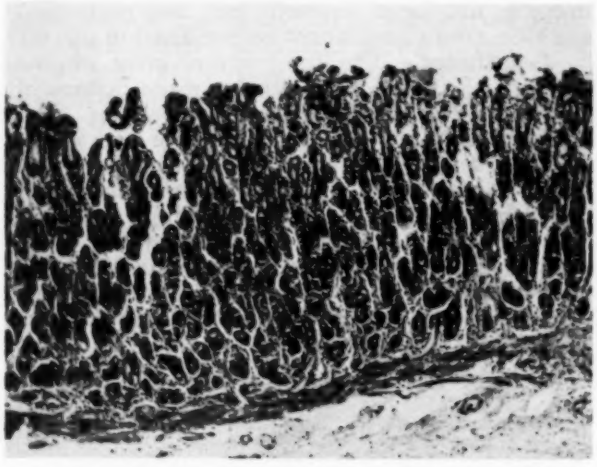

FIG. 489.—Section from œsophagus below the stricture. Mucosa resembles that found in the stomach. (× 75.)

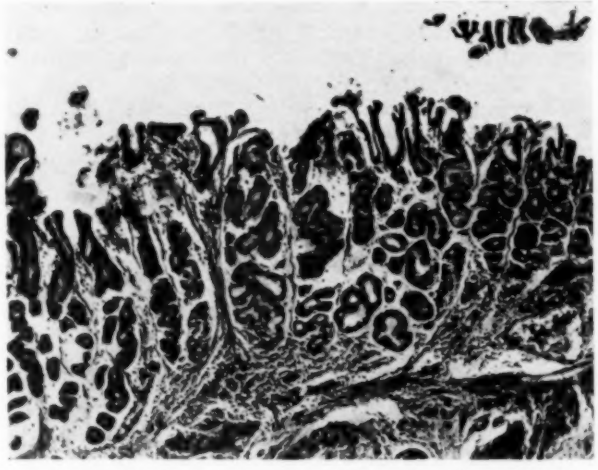

FIG. 491.—Section from œsophagus below the stricture. The glands are arranged after the pattern found at the pyloric end of the stomach. The cells are basophil. No parietal cells are present. (× 75.)

This type of anastomosis is satisfactory as part of the palliative œsophagectomy for carcinoma at this level, but when operation carries with it a long expectation of life the jejunum is preferable to the stomach for the restoration of the continuity of the alimentary canal. The regurgitation of acid gastric juice with consequent œsophagitis is thereby prevented, as Allison has emphasized. When it was seen that the lesion was due to œsophagitis at the junction of œsophageal and gastric mucosæ, recurrence of stricture was awaited with trepidation. Symptoms returned soon after the patient returned home, but were at first relieved by dilatations. Severity of symptoms determined his re-admission to hospital six months after his first operation.

On May 27, 1954 the first operation was completely undone, the stomach returned to the abdomen and an end-to-side jejuno-œsophagostomy performed after the manner of Roux. Despite several complications he made eventually a good recovery. He is now well (Feb. 1, 1955) with no dysphagiæ, a satisfactory anastomosis and a rapid increase in weight. (*See Fig.* 488.)

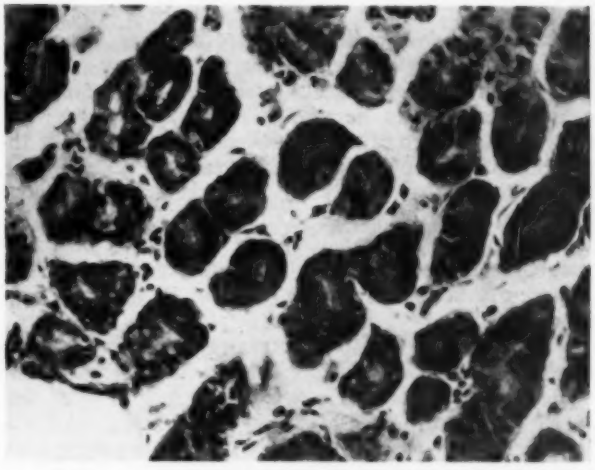

FIG. 490.—Sections from œsophagus below the stricture showing 'gastric' glands cut across. Parietal cells appear active and functional. (× 150.)

FIG. 492.—Section from œsophagus below the stricture, showing villi. (× 75.)

DISCUSSION

Age of Onset.—Œsophageal regurgitation of gastric contents is all too common, as any man unaccustomed to handling small babies finds to his cost. Allen (1950) states that this can frequently be demonstrated radiologically. His view does not support that of Berenberg and Neuhauser (1947), who found only 12 out of 2000 infants with relaxation at the œsophageal opening.

Wyllie and Field (1946), Findlay and Brown Kelly (1950), and Allison (1948) have described œsophagitis with stricture formation in children. In all these cases the causative lesion was considered to be œsophageal hiatus hernia with acid regurgitation.

Whatever the cause of the regurgitation it may determine the onset of œsophagitis, as many surgeons have now recorded. Some will not agree with Gross

(1953), who has described œsophagitis and œsophageal stricture otherwise so accurately, that " the development to a cicatricial form is very slow : it is seldom seen in childhood, and is largely a problem of adult life ". There are many instances of stricture recorded in infancy and childhood, such as those of Findlay and Brown Kelly (1950), Beatty (1928), Sheldon and Ogilvie (1929), and Belsey (1954), the child described by the last named being six weeks old. In all of these cases the commonest cause of the œsophagitis initiating stricture formation was œsophageal hiatus hernia.

Stricture formation or, at least, narrowing of the œsophagus can occur in the absence of œsophagitis, and Gross (1953, p. 110) has treated 38 patients suffering from " congenital esophageal stenosis ". This was the diagnosis made by us in the case recorded in this paper. It is possible that other apparently ' congenital ' lesions may be inflammatory in origin.

Histology.—Various examinations at different times showed that the œsophagus was divided into two halves by the stricture. The upper part was lined by stratified squamous epithelium and the lower by a mucous membrane varying in appearance from place to place but mainly gastric in general pattern.

Several details seemed important. Firstly the stricture was an inflammatory one and not a congenital atresia. The muscle coats were broken up by fibrous tissue. In areas there were collections of neutrophil leucocytes, evidences of vascular reaction, and œdema. The epithelium immediately below the stricture (*Fig.* 489) resembled that found in the stomach at its fundal end. Parietal cells (*Fig.* 490) were abundant and appeared capable of full physiological activity. In other areas the mucous membrane simulated that seen at the pyloric end of the stomach (*Fig.* 491). The staining reactions were identical and suggested that these areas produced an alkaline secretion.

In several areas (*Fig.* 492) there were villi similar to those found in the intestine. Between these there were small crypts. The cells here were mainly basophil. While the stricture divided the columnar from stratified squamous epithelium, the inflammatory reaction appears to involve the gastric type of epithelium more than the squamous.

In the absence of any demonstrable reflux at the cardiac end of the œsophagus, it appears possible that the œsophagus itself, in this case, could produce enough acid gastric juice to establish a cicatrizing œsophagitis. Stewart and Hartfall (1929) commented on the abundance of oxyntic cells in the patches of gastric mucosa they found at the upper end of the œsophagus.

The presence of intestinal villi in the œsophagus is perhaps an answer to those who would always look for a mechanical explanation for developmental abnormalities. Gastric mucous membrane in this situation might be due to a short œsophagus and a stomach misplaced upward, but the presence of intestinal epithelium cannot be explained in this way.

Treatment.—The fundamental error of using stomach for this anastomosis was made because the lesion was thought to be congenital atresia. Even had it been so the jejunum should have been used.

At the second operation the stomach was replaced into the abdomen and used for gastrostomy feeding. We found very helpful an electrical liquidizing unit, sold as a domestic appliance, which renders all manner of food, solid or otherwise, into a thin gruel capable of passing down even a fine tube. Treating the food in this way was a remarkable advance in the management of the patient.

SUMMARY

A case of cicatrizing œsophagitis is described in a boy aged 9 with symptoms commencing at birth.

The œsophagus below the stricture was lined by an epithelium which was mainly gastric in pattern, but in places was of intestinal type.

In the absence of hiatus hernia or demonstrable reflux it is suggested that the gastric mucous membrane in the œsophagus might initiate œsophagitis.

The photographs were prepared by Mr. Woodwood-Smith, University of Sydney.

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ŒSOPHAGEAL CARCINOMA COMPLICATING ACHALASIA OF THE CARDIA

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ACHALASIA of the cardia complicated by œsophageal carcinoma is rarely seen, and published case reports show that early diagnosis presents exceptional difficulties. Two cases are here described, with a review of the literature.

CASE REPORTS

Case 1.—A housewife, aged 54, first attended hospital in July, 1953. She had complained of dysphagia and regurgitation of undigested food for twenty-five years, but had maintained otherwise good health until May, 1953. Since then there had been frequent vomiting of brown fluid, and all food had provoked regurgitation, coughing, and choking attacks. She had lost weight rapidly, and had noticed that her voice had become slightly hoarse at times. She was wasted and dehydrated. The trachea was displaced to the right and there were dullness to percussion and diminished breath-sounds over the right upper zone of the chest anteriorly.

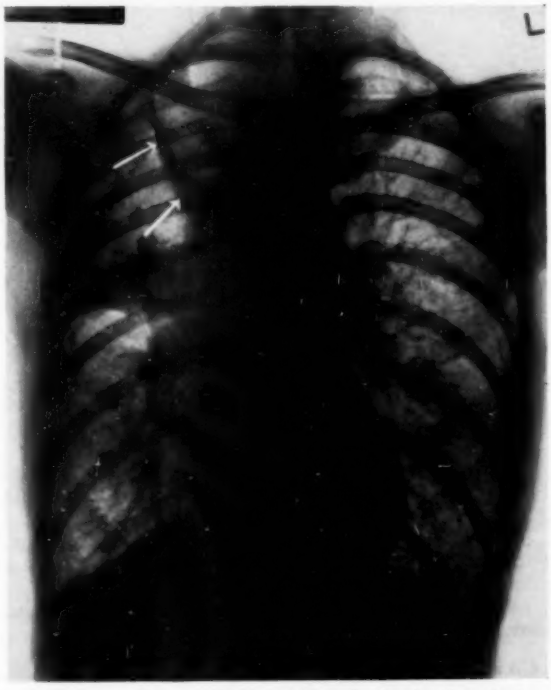


FIG. 493.—*Case* 1. Chest radiograph showing broadening of the mediastinum. The arrows indicate the thickened œsophageal wall crossing the right upper zone.

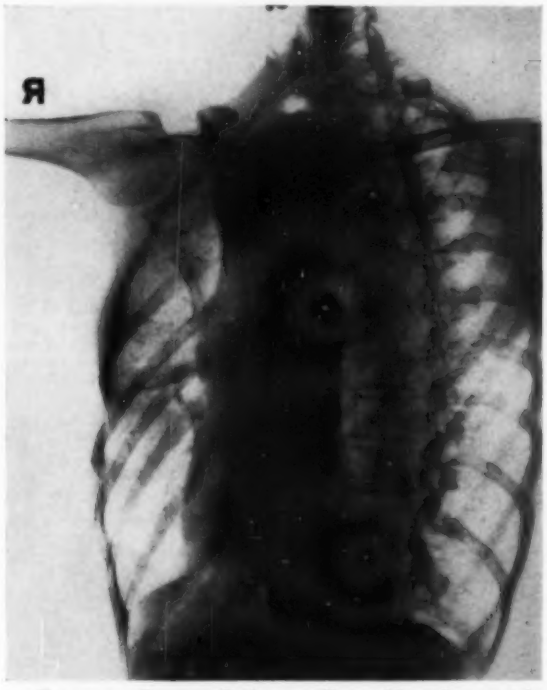


FIG. 494.—*Case* 1. Barium swallow. Note the constriction in the upper œsophagus, with dilatation above and below.

A chest radiograph (*Fig.* 493) showed a coarse opacity running obliquely downwards and inwards across the right upper zone, and merging with the mediastinal shadow. This appeared to enclose gas, and at fluoroscopy with barium swallow it was confirmed as being the œsophageal wall. The whole œsophagus was seen to be grossly dilated and elongated, but there was a persistent localized constriction of the lumen opposite the bodies of D.5 and D.6 (*Fig.* 494). Spill-over of opaque medium into the larynx occurred during the second stage of deglutition. Tracheal displacement to the right, and pneumonic changes at the right base were also described.

Œsophagoscopy was performed and quantities of food and stagnant secretion were removed by suction. The lumen was enormously wide at all levels below the cricopharyngeal sphincter, and no growth was found. The cardia was dilated with bougies.

With out-patient treatment there was an initial improvement, but after an interval her general condition deteriorated again. When re-admitted to the ward in December, 1953, she was unable to swallow fluids because of the choking attacks provoked by inhalation. Indirect laryngoscopy showed complete paralysis of the left vocal cord and impaired abduction of the right cord. A further radiograph (*Fig.* 495) revealed anteroposterior compression of the trachea at the level of the manubrium sterni. Bronchoscopic examination confirmed this observation, the lumen being stenosed at a level 2 in. above the carina. There was no œsophagotracheal fistula. Œsophagoscopy was again performed, and again no growth was found.

AT OPERATION.—Left thoracotomy was undertaken, after correction of dehydration by intravenous saline and blood transfusion. The œsophagus was greatly dilated from the diaphragm up to the aortic arch. Above this was a hard tumour mass, infiltrating the upper mediastinum, and fixed to the trachea, aorta, and prevertebral fascia. Heller's operation was completed in the hope of improving œsophageal drainage into the stomach, and facilitating radiotherapy on a fitter patient. At the end of the operation the poor airway through the stenosed trachea gave rise to cyanosis. A Portex endotracheal tube was therefore inserted through a low tracheotomy opening, and passed to a level below the stenosis. This

maintained a good airway, and allowed easy aspiration of bronchial secretions. The patient recovered consciousness, but relapsed a few hours later and died.

FIG. 495.—*Case* 1. Lateral view showing the stenosis of the tracheal lumen.

FIG. 497.—*Case* 2. Chest radiograph showing broadening of the mediastinum. Thickened œsophageal wall is visible to the right of the heart shadow.

AT AUTOPSY (Dr. C. Keith Simpson).—Two cm. below the cricoid cartilage was the upper edge of an ulcerated œsophageal carcinoma 10 cm. in length. The growth invaded the walls of the œsophagus and of a large lateral pouch on the right side (*Fig.* 496). In the midline the prevertebral fascia and the posterior tracheal wall were invaded, but there was no œsophagotracheal fistula.

FIG. 496.—*Case* 1. The œsophagus at autopsy. The arrow indicates where the trachea has been opened from behind to show invasion of its posterior wall.

At all levels the œsophageal lumen was considerably wider than normal. There were two small diverticula in the lower third. The cardia itself was normal.

The lungs showed numerous areas of suppurative bronchopneumonia. The other organs were normal and no metastases were present.

Sections of the tumour showed a lightly keratinized squamous carcinoma.

Case 2.—A waiter, aged 43, first sought medical advice in January, 1954. He had suffered from intermittent difficulty in swallowing for twenty years. Whenever food had become stuck it had had to be regurgitated. Appetite had always been good, however, and weight steady at 14 st. until early December, 1953, when food became consistently difficult to swallow, solids more so than liquids. There were occasional attacks of coughing and choking whilst eating, and it had become more difficult to regurgitate back his food. He never brought up blood and had had no pain. He was well nourished, with no abnormality on clinical examination apart from tracheal displacement to the right. The pharynx and larynx were normal to mirror examination.

A chest radiograph showed broadening of the mediastinum, and the thickened œsophageal wall to the right of the heart shadow (*Fig.* 497). Patchy parenchymal changes with possibly some lower-lobe collapse were seen at the right base. During barium-swallow fluoroscopic examination achalasia of the cardia with œsophageal dilatation above it was observed (*Fig.* 498). Throughout the examination, however, the œsophagus at the level of D.1 and D.2 appeared consistently narrowed (*Fig.* 499). This narrowing, associated with the broadening of the mediastinal shadow at the same level, caused the

radiologist to query whether carcinoma might have supervened.

Œsophagoscopic examination was carried out and a large ulcerated growth encircling the œsophagus and reaching upwards to the cricopharyngeal region was found. The lumen was stenosed and the instrument could not be passed farther. Examination of biopsy material showed a lightly keratinized squamous carcinoma.

FIG. 498.—*Case* 2. Œsophagus, cardia, and stomach at barium swallow.

AT OPERATION.—Right thoracotomy was done and the lower œsophagus was found to be greatly dilated. There was a large neoplastic mass in the upper mediastinum, fixed to the vertebral column and the great vessels. It was clearly inoperable. After closure of the chest œsophagoscopy was performed and the malignant stricture was dilated with bougies. The patient made a good recovery, and as a result of the dilatation swallowing has become easier. At the time of writing no other palliation seems indicated.

DISCUSSION

Before the thoracotomy was done in *Case* 1 the presence of carcinoma was not thought likely because of negative endoscopy findings. The importance of circumstantial evidence, in the changed pattern of the dysphagia, recurrent laryngeal nerve paralysis, tracheal compression, and persistent localized constriction of the œsophagus, was overlooked. The failure to find growth at œsophagoscopy is attributed to the very wide œsophageal lumen, even at the level of the tumour, which permitted a tube to pass unhindered, and to failure to wash out the œsophagus adequately beforehand. The appearances were masked by retained food and secretion. It was hoped that the tracheal compression and recurrent laryngeal palsy might be due to the mechanical pressure of the dilated œsophagus. This growth must already have been very large when the patient was first seen, and if it had been recognized gastrostomy might have been performed as a better means of palliation.

In *Case* 2 the growth had extended into the cervical part of the œsophagus, which was not dilated as a result of the achalasia. Stricture was therefore present and the diagnosis was easy (*Fig.* 500). Nevertheless the intrathoracic part of the tumour must have been present for some time before the patient sought advice.

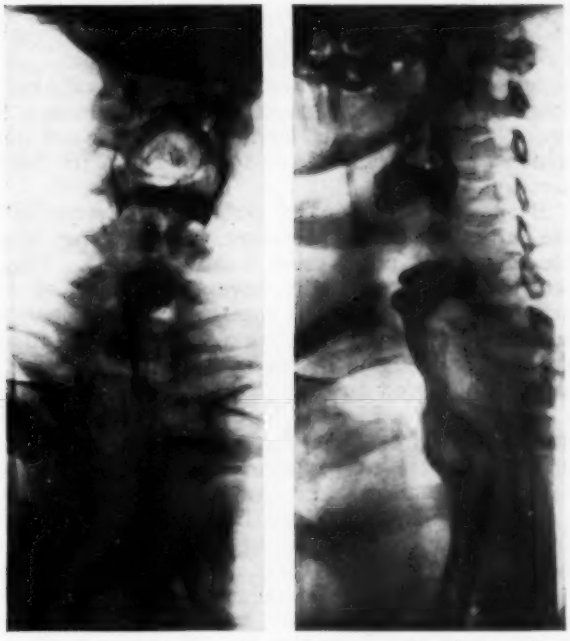
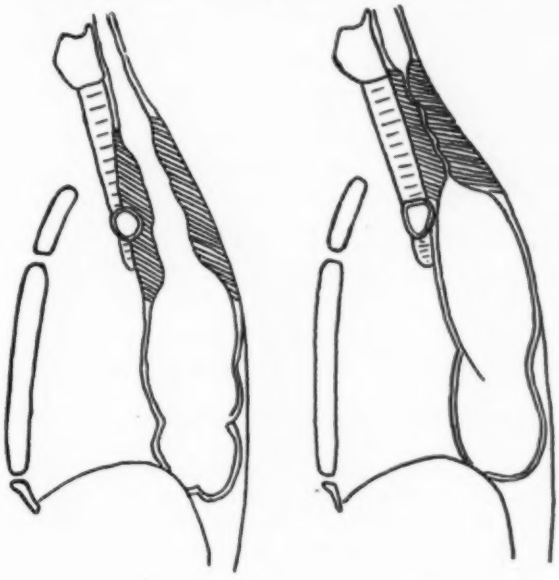


FIG. 499.—*Case* 2. Postero-anterior and oblique radiographs at barium swallow, showing persistent stenosis of the upper œsophagus immediately above the dilated portion.



1 2

FIG. 500.—To illustrate that mechanical obstruction was absent in *Case* 1 but very marked in *Case* 2.

The question arises whether anything can be done in the management of achalasia to detect such growths in an operable stage, and a brief review of the

literature is necessary in order to give a proper perspective in this connexion. Attention was drawn by Rake (1931) to the effects of stagnation of food in the œsophagus in achalasia. He described the ulceration and attempted healing with papillomatous overgrowth of the epithelium, and regarded the long-standing irritation as a dangerous condition predisposing to carcinoma. He mentioned 4 cases of malignancy supervening on achalasia, and suggested that this complication is by no means rare. Thorough medical treatment and œsophagoscopy at regular intervals were advocated to reduce the incidence of carcinoma and to ensure its early detection.

Baer and Sicher (1947) published a report of a case and reviewed the literature, in which they were able to trace 8 other cases fully described. Since then reports of 4 others have appeared, and all authors have regarded as rare the development of carcinoma in achalasia. Mathews and Vinson (1950) state that it occurred in only 3 out of 1000 cases of achalasia observed by them. Mention of it is made in only two of a number of major text-books consulted. Rake's opinion that this complication is a common one is not supported by the literature, therefore, and until more case records are available it seems reasonable to adopt the view that the risk of carcinoma supervening in cases of achalasia is not likely to be greater than it is in the general population.

Symptoms.—An unexplained deterioration in the general condition may be the first and only indication that carcinoma has developed. It is particularly important to realize that the pattern of the dysphagia to which the patient has been accustomed for so many years will not be appreciably altered while the growth is confined to the widely dilated part of the œsophagus. Only when the cervical œsophagus or the recurrent laryngeal nerves are involved does the swallowing become more difficult. In the published cases, including the two here reported, the following late symptoms occurred :—

Cough aggravated by attempts to swallow. In some cases this was due to œsophagotracheal fistula, in others to inhalation at the laryngeal inlet	6
Recent severe loss of weight	5
Increased dysphagia	5
Œsophageal bleeding	3
Vomiting, as distinct from regurgitation	3
Retrosternal pain	2
Hoarseness due to recurrent laryngeal paralysis	1
Hæmoptyses	1

Special Investigations.—Diagnosis of a carcinoma in the dilated œsophagus is bedevilled by numerous factors, besides the absence of additional symptoms in the early stages. The first of these factors is the emphasis traditionally laid upon the differential diagnosis between achalasia and growths of the lower end of the œsophagus. Gore and Lam (1952) refer to this, and to the natural relief of anxiety which is usual when achalasia is found at radiological and endoscopic examinations. They stress that the necessity of excluding growth remains even when achalasia is found. It is essential to realize that careful study of the entire length of the œsophageal walls is called for, as shown by the fact that in the published cases, including those here described, 3 growths were in the upper third, 11 in the middle third, and only 3 in the lower third.

Baer and Sicher (1947), Kornblum and Fisher (1940), and Bersack (1944) have all described the difficulties in diagnosis by barium swallow X-ray studies. They point out that spurious filling defects due to retained food are commonly seen and that satisfactory shadows can only be obtained after thorough evacuation of the œsophageal contents. The two cases here described show that any relative narrowing of the lumen which is not clearly due to the kinking of an elongated œsophagus must be regarded as highly suspicious of a superimposed carcinoma.

With regard to œsophagoscopy, all authors have regarded this as the critical investigation which cannot be omitted in any case of achalasia. Rake (1931), Gore and Lam (1952), and Kastl (1953) suggest that it might be done at regular intervals in order to detect otherwise unsuspected growths. *Case* 1 reported here illustrates all too clearly that even direct endoscopy can fail to demonstrate a large tumour when the œsophagus is dilated, and is obscured with retained food and secretion.

Evidence of œsophageal bleeding was stated by Kornblum and Fisher (1940) to be suggestive of malignant change, and tests for occult blood in the stools may be of some value in this connexion. It must be remembered, however, that shallow erosions and healing ulcers as described by Rake are seen in the œsophageal wall in uncomplicated achalasia. These may give rise to bleeding, which, however disquieting it may be, cannot be taken to indicate the presence of a growth.

CONCLUSIONS

Carcinoma is a rare complication of achalasia. Until more case records are available it cannot be said whether there is any statistical basis for regarding achalasia as a ' precancerous ' condition. In view of the exceptional diagnostic difficulties which are discussed above, it seems probable that some cases pass unrecognized when œsophagoscopy or autopsy is not performed.

It is counsel of perfection to advocate routine œsophagoscopy at regular intervals in all cases of achalasia, in order to detect a complication so far described in fewer than 20 cases. In order to arrive at a clearer idea of the frequency of this complication, and in an endeavour to detect growths in an operable stage it seems desirable to re-emphasize the following points :—

1. The radiological diagnosis of achalasia does not mean that carcinoma is not present. With care most of these growths could be suspected at barium swallow, and this examination should always be repeated after thorough œsophageal lavage, when achalasia is first discovered at fluoroscopic examinations.

2. Œsophagoscopy is essential in the initial assessment of a case of achalasia, and should only be performed after thorough aspiration and lavage. A growth is easily overlooked in the dilated œsophagus.

3. Growth may arise at any level, and the region of the cardia must not be allowed to divert attention from the higher parts of the œsophagus.

4. Periodic observation of patients with achalasia is essential. In some of the recorded cases periods

years without follow-up occurred, and patients finally returned with inoperable growths.

5. During follow-up, cough due to inhalation of food and fluids, evidence of œsophageal bleeding, or change in the pattern of dysphagia should result in full re-investigation of the case as a matter of urgency.

I am grateful to Mr. L. L. Bromley for permission to report *Case* 1, and to H.M. Coroner for the Western District of London for permission to report the post-mortem findings. Dr. E. Neumark kindly wrote the description of the autopsy appearances, and prepared the specimen, which was photographed in the Photographic Department of St. Mary's Hospital. My thanks are due to Mr. A. Dickson Wright for permission to study and report *Case* 2, and to Dr. E. Rohan Williams for his guidance on the radiological aspects of this subject.

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A CASE OF CONGENITAL ŒSOPHAGEAL DIVERTICULUM, LOWER ACCESSORY LOBE, AND ŒSOPHAGOBRONCHIAL FISTULA

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IN the case about to be described there existed a lower accessory lobe of lung, a congenital epiphrenic œsophageal diverticulum, and an œsophagobronchial fistula. The case is of interest because of its rarity and, more especially, because of its implications in the development of certain intrathoracic congenital malformations.

CASE REPORT

The patient, a boy 16 years of age, was first seen at the Thoracic Surgical Department on April 1, 1955. A chest radiograph two years before had been reported as normal. The boy had been healthy until November, 1954, when he had a febrile illness diagnosed as influenza. His symptoms were severe cough and epigastric discomfort. A chest radiograph at that time showed an opacity at the base of the left lung. On the lateral film the opacity appeared to lie in the posterior basal segment. Symptoms persisted and he was seen by a physician at hospital. Radiological examination with a barium meal showed a diaphragmatic hiatal hernia. Inflammatory changes at the base of the left lung were noted. In view of the diagnosis of hiatal hernia, the patient was referred to the Thoracic Surgical Department.

The patient complained of cough, which came in violent bouts culminating in vomiting. The cough was related to posture and to swallowing. Sometimes the cough would come on during a meal, and at other times did not begin until immediately after a meal. It was troublesome during the night, but came on only when he lay on his back or on his left side. He could prevent the cough by lying on his right side. He expectorated 1 oz. of mucopurulent sputum daily. No swallowed material had been recognized in the sputum. Symptoms were intermittent and had been less troublesome during the three weeks before this examination.

On physical examination the boy looked well and was well developed. There were no abnormal physical signs to be found on examination of his chest. There was no evidence of infection in the upper respiratory tract.

Further radiological studies were carried out. Postero-anterior and lateral films of the chest showed persistence of the opacity at the left base. Penetrating films demonstrated the presence of numerous cystic spaces within the opacity. Tomography revealed more clearly the presence of these small cysts and also the presence of a larger cyst-like space measuring 3 cm. in diameter. Bronchography demonstrated the presence

FIG. 501.—Barium swallow showing the œsophageal diverticulum and the opacity caused by the lower accessory lobe.

of a normal bronchial tree on the left side, apart from the fact that the left lower lobe bronchi did not enter the area of the opacity previously noted. There was no evidence of bronchiectasis. No opaque medium was seen to enter

the œsophagus. On barium swallow examination (*Fig.* 501), the barium was seen to leave the œsophageal lumen and to fill, in an irregular manner, a space lying on the left side of the œsophagus immediately above the diaphragm. Occasionally reflux of barium could be made to occur from the stomach through the cardia, and

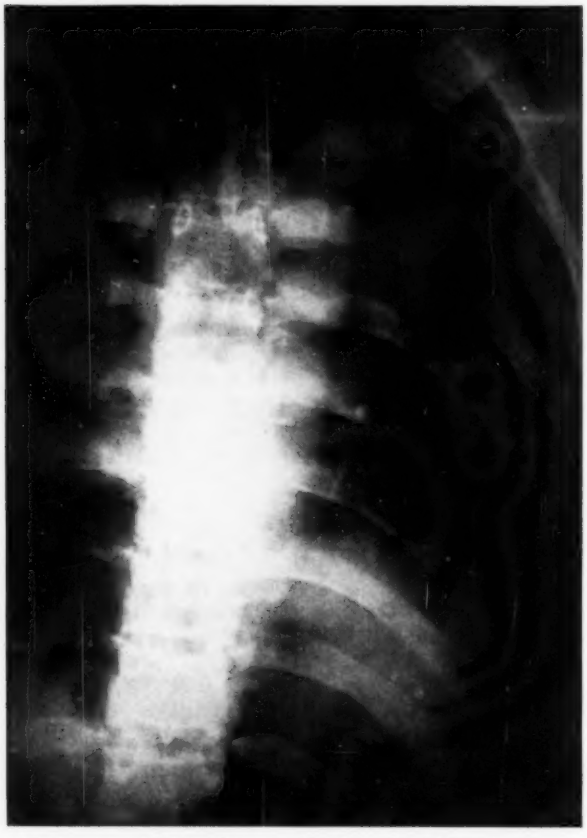

FIG. 502.—Angiocardiogram showing the aberrant artery (indicated by the arrow) to the accessory lobe.

again irregular filling of a space lying to the left of the lower part of the œsophagus was seen to occur. Barium did not enter the bronchial tree. Lipiodol swallows with the patient lying on his back and on his left side also failed to show an œsophagobronchial fistula.

On bronchoscopy the only abnormality seen was mucosal inflammation in the left lower-lobe bronchus. No abnormality was seen on œsophagoscopic examination.

As the presence of an opacity containing cystic spaces and lying in the lower part of the chest suggested the presence of a congenital malformation of lung, angiocardiography was performed (*Fig.* 502). By this means an aberrant artery was demonstrated. The vessel proceeded upwards from the abdominal aorta at the level of the first lumbar vertebra to the opacity at the base of the left lung.

From the clinical history and the radiological examination it was thought that the œsophagus was communicating with an accessory lobe of lung and that an œsophagobronchial fistula existed.

AT OPERATION (May 24).—A left thoracotomy was carried out. The upper and lower lobes appeared to be normal apart from an impression on the lower lobe caused by a firm fleshy mass lying immediately above the diaphragm in the posterior part of the left side of the chest and presumed to be a lower accessory lobe of lung. The accessory lobe was attached to the parietal pleura of the chest wall by dense adhesions and to the diaphragm by slender adhesions. It was easily separated from the lower lobe by gauze dissection, except at one point where it was connected with the lower lobe by a pedicle. In this pedicle there was a large vein which coursed upwards and medially to join the inferior pulmonary vein. The pedicle also contained a band of tissue which felt firm and was thought to contain a small bronchus. The vein was

FIG. 503.—Photograph of the resected specimen.

divided between ligatures. A patent bronchus could not be demonstrated in the pedicle. A portion of this tissue was removed for histological examination. Dissection was then carried out in the direction of the œsophagus. On the posterior aspect of the accessory lobe an area was encountered which had the appearance of a portion of bowel. At this stage the œsophagus was mobilized above the accessory lobe and also immediately above the cardia. A vessel, about the size of a normal adult axillary artery, was found coming through the diaphragm in the region of the left crus. This artery was divided between ligatures. It then became apparent that there was a diverticulum of the œsophagus embedded in the accessory lobe. The neck of the diverticulum was easily displayed. Its surface was smooth and the œsophageal muscle was seen to continue into the wall of the diverticulum. There were no inflammatory adhesions present around the neck of the diverticulum. There were, however, two firm enlarged glands one above and one below the neck of the diverticulum. The neck of the diverticulum was divided. Its opening into the œsophagus was about 1 cm. in length and 0·5 cm. in width. The mucosa and submucosa in this region showed no evidence of inflammation or ulceration on macroscopical examination. The opening in the œsophagus was closed with two layers of catgut suture.

The patient made an uneventful recovery. His cough was immediately relieved.

PATHOLOGY.—The resected specimen (*Fig.* 503) measured 11 × 7·5 × 6 cm., and consisted of an accessory lobe of lung, almost completely embedded in which was an œsophageal diverticulum. A large vessel entered the accessory lobe on its inferior aspect. The vessel divided into two branches, which passed one in front of and one behind the diverticulum, giving off small branches to the diverticulum, and then being distributed throughout the accessory lobe. A pedicle emerged from

the superomedial aspect of the accessory lobe. It contained a vein and, in addition, some tissue the nature of which was indeterminate on naked-eye examination. The neck of the diverticulum was smooth on its external surface. The muscle of the œsophagus was continued into the wall of the diverticulum. The mucosal surface away from its neck (*Fig.* 504) was similar, but more of the muscle layer was replaced by fibrous tissue. The diverticulum lay in a bed of fibrous tissue which contained large vascular spaces and merged gradually into the tissue of the accessory lobe. Histological examination of the wall of the track by means of which the

FIG. 504.—Photomicrograph of the wall of the diverticulum. (× 9·6.)

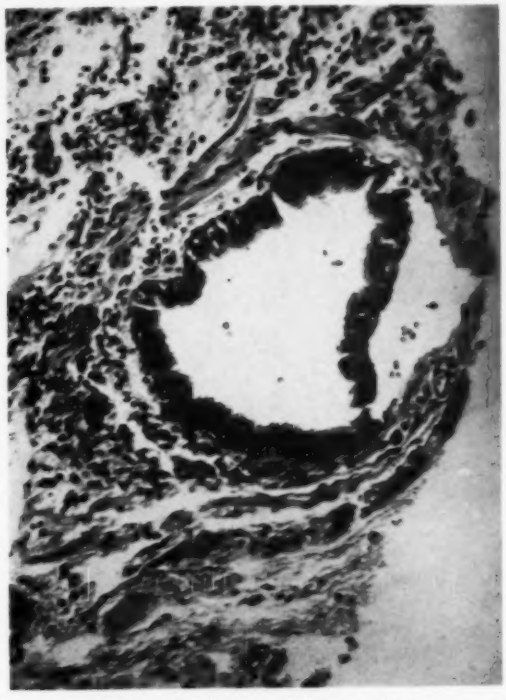

FIG. 505.—Section showing one of the bronchioles connecting the accessory lobe to the left lower lobe. (× 30.)

of the neck of the diverticulum was intact. The diverticulum was 5 cm. in diameter. Its lining was glistening, and showed no sign of ulceration. The diverticulum communicated with the interior of the accessory lobe by means of a small channel which admitted a probe for a distance of 1·5 cm.

Section of the specimen showed the accessory lobe to contain numerous small cystic spaces, and one larger space of irregular shape and having the appearance of a distended bronchus. The track from the diverticulum into the accessory lobe could be followed for a short distance only. Thereafter it became lost in the irregular structure of the lobe. The œsophageal diverticulum could be peeled out of the accessory lobe with some difficulty, leaving a smooth bed of fibrous tissue.

Histology.—The accessory lobe showed a honeycomb structure of cystic bronchi lined by epithelium varying from ciliated columnar to flattened cuboidal. The contents of the cysts consisted of serous fluid with varying admixture of blood, leucocytes, macrophages, and giant cells. The stroma was fibrous, with many congested blood-vessels and numerous inflammatory cells with some lymphoid follicles. In some areas there were lung alveoli distended with serous fluid and macrophages.

The diverticulum near its neck showed a lining of pseudo-stratified ciliated columnar epithelium. The wall had a well-formed muscle layer broken up by fibrosis, scattered bronchial glands, and small cysts. There was considerable submucosal infiltration with inflammatory cells, mainly plasma-cells. There were numerous congested capillaries in the submucosal layer. The structure of the wall of the diverticulum further

FIG. 506.—Photomicrograph of the wall of a large cystic space within the accessory lobe. (× 40.)

diverticulum communicated with the interior of the accessory lobe showed a lining of ciliated columnar epithelium deep to which there were cartilage, glands of bronchial type, and dense fibrous tissue containing numerous capillaries and infiltrated with lymphocytes and plasma cells.

Section of the band of tissue accompanying the vein which drained the accessory lobe showed the presence of several bronchioles (*Fig.* 505).

appearances of the wall of the diverticulum differed from those of the wall of the larger cyst lying within the accessory lobe. The clinical history suggested recent inflammation in the accessory lobe. This was confirmed radiologically. It seemed probable that the communication between the diverticulum and the left lower lobe arose as a result of an acute inflammatory process within the accessory lobe.

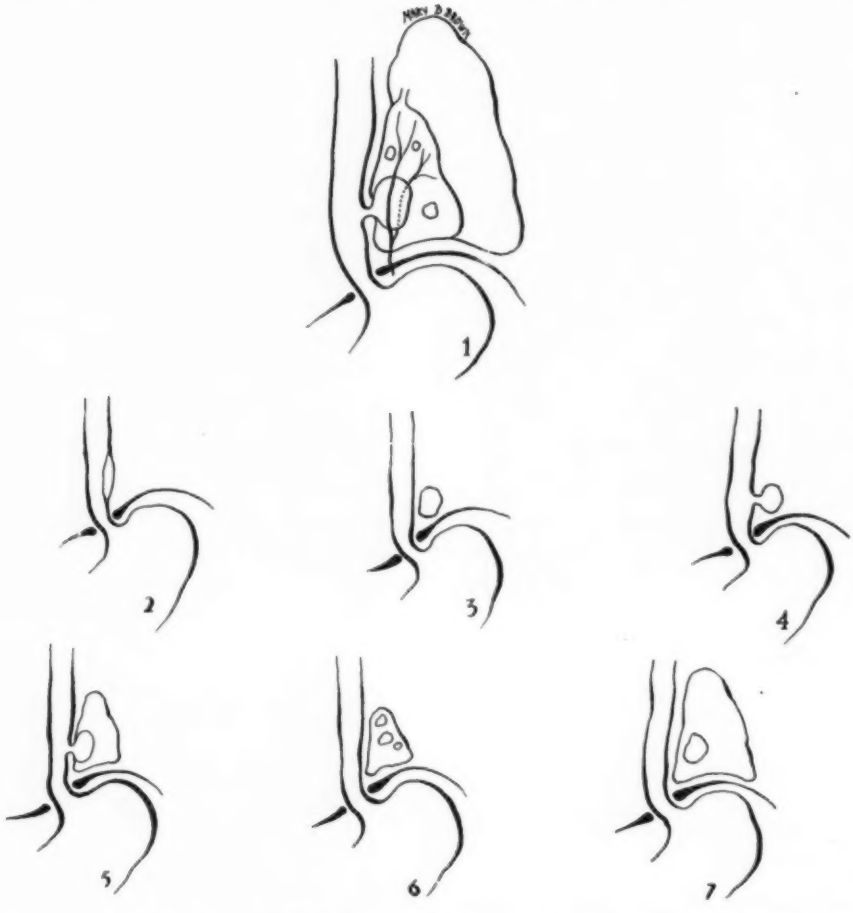

FIG. 507.—1, Diagram of the case described in this report; 2-6, Analysis of the types of lesion coexisting in this case together with certain apparently analogous lesions; 2, Intramural ciliated epithelial cyst of the œsophagus; 3, Mediastinal ciliated epithelial cyst; 4, Congenital epiphrenic œsophageal diverticulum; 5, Congenital epiphrenic œsophageal diverticulum in association with a lower accessory lobe; 6, Lower accessory lobe containing cysts lined by ciliated epithelium; 7, Congenital lung cyst.

Section of the artery to the accessory lobe and the diverticulum showed a moderate-sized artery with some thickening of the intima and reduplication of the internal elastic lamina.

Both of the glands lying in relation to the neck of the diverticulum showed simple lymphoid hyperplasia.

Fig. 506 is included to show the difference in structure between the wall of the œsophageal diverticulum and the wall of a large cyst within the accessory lobe.

DISCUSSION

There was no evidence that a cystic space within the accessory lobe had ruptured into the œsophagus. The neck of the diverticulum was smooth and free from inflammatory adhesions on its external aspect. Furthermore the œsophageal muscle was seen macroscopically and microscopically to be continued into the wall of the diverticulum. The histological

The existence of an œsophagobronchial fistula was not proved radiologically, which is not surprising as only bronchioles of small calibre were found in the pedicle joining the accessory lobe to the left lower lobe. Judging from the clinical history, an œsophagobronchial fistula existed which was patent intermittently. Before operation severe bouts of coughing were related both to swallowing and to posture. After operation, cough immediately disappeared. The history of œsophagobronchial fistula was of short duration, and the fistula was dealt with before bronchiectatic changes occurred in the left lung.

Epiphrenic diverticula of the œsophagus are relatively uncommon. They are usually of pulsion type. Some are congenital. Baar and d'Abreu (1949) described a case of congenital epiphrenic

œsophageal diverticulum which contained pancreatic tissue in its wall, and the blood-supply of which was derived from an aberrant branch of the abdominal aorta. The diverticulum described in the present report was also congenital in origin, and again its blood-supply was derived from an aberrant vessel arising below the diaphragm.

It is not our purpose to discuss the various theories which have been put forward to explain such abnormalities as accessory lung, congenital lung cysts, and certain mediastinal cysts. On the one hand there is the theory of sequestration of a portion of developing lung bud by pleural adhesions, as suggested by Rektorzik (1861), or by an aberrant vessel, as suggested by Pryce (1946). On the other hand, Eppinger (1904) considered that such lesions arise from supernumerary buds of the foregut, such buds being capable of varying degrees of self-differentiation and being potentially capable of forming respiratory tissue. Certain cases are perhaps best explained by the latter theory. Scheidegger (1936) described a case of accessory lung which communicated with the stomach by means of a gastric diverticulum lined by gastric mucosa. Gans and Potts (1951) described an anomalous lobe of lung arising from the œsophagus. Our case belongs to this group. When, as in these cases, an accessory lobe communicates with the intestinal tract, there seems to be good evidence that the accessory lung tissue and the communicating track or diverticulum have arisen as an independent bud from the foregut, this bud having respiratory potentials. It is difficult to explain such cases according to a sequestration theory.

An acquired œsophageal diverticulum may rupture into a bronchus and give rise to bronchiectasis. Bronchiectasis in association with a congenital œsophageal diverticulum must be considered to be possibly of congenital origin. In the case described by Baar and d'Abreu the diverticulum was congenital. It did not communicate with a bronchus. Bronchiectasis existed in the adjacent lung. They observed that the histological findings were " suggestive of congenital malformation of the bronchial tree ". In our case there was no doubt about the congenital nature of the pulmonary malformation associated with the congenital œsophageal diverticulum. Monod (1949) described 3 cases of epiphrenic diverticulum of the œsophagus communicating with a bronchus and associated with lung abscess. In each case the diverticulum showed no evidence of having arisen as a result of an inflammatory lesion. The wall of the diverticulum was in each case of the same structure as the œsophagus. These diverticula were possibly congenital in origin. The lung abscess was in each case resistant to treatment. In the second and third cases the abscess persisted in spite of treatment with penicillin and surgical obliteration of the fistula. Again the possibility exists that the pulmonary lesions in these cases were congenital in origin.

Baar and d'Abreu described 5 cases, including the case of congenital epiphrenic œsophageal diverticulum, all of which they considered to be due to failure of resorption of accessory buds of the primitive foregut. These cases were a left superior accessory lung, a right ' tracheal ' accessory lung, an œsophageal epiphrenic diverticulum, an intrapericardial teratoid tumour, and a ciliated epithelial œsophageal cyst. In the present case a number of these anomalies are combined, emphasizing their common developmental origin. On analysis of this case it is possible to separate the following types of lesion : (1) Accessory lobe of lung ; (2) Congenital lung cysts (in this case lying within the accessory lobe) ; (3) Congenital œsophageal diverticulum ; and (4) As the œsophageal diverticulum was lined by ciliated columnar epithelium, it would seem to bear a close relationship to ciliated epithelial cysts either within the œsophageal wall or in the adjacent mediastinum.

Fig. 507 is a diagrammatic representation of the above analysis of the case illustrating the suggested common developmental origin of these lesions from a supernumerary bud of the primitive foregut.

It is of interest that in most cases previously described the mucosal lining of a tubular malformation in continuity with the intestine was of the same type as that present in the portion of the intestine with which it communicated. This was true of the cases described by Scheidegger (1936) and Baar and d'Abreu (1949). That the fact of continuity does not necessarily mean that the two mucosæ will be the same is suggested by the case of Gans and Potts (1951) in which the accessory lobe communicated with the œsophagus by a tube lined by columnar epithelium, and by our case in which the œsophageal diverticulum was lined by ciliated columnar epithelium.

SUMMARY

A case is described of lower accessory lobe of lung, congenital epiphrenic œsophageal diverticulum, and œsophagobronchial fistula. The embryological implications of the coexistence of these anomalies in a single case are discussed.

I am indebted to Dr. H. S. Kellett for the pathological reports, and to Miss M. B. Brown and Mr. P. Harrison for the illustrations.

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MEGALOBLASTIC ANÆMIA FOLLOWING GASTRIC RESECTION

REPORT OF TEN CASES

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A MACROCYTIC anæmia clinically and hæmatologically indistinguishable from Addisonian pernicious anæmia has been reported many times following total gastrectomy in man, and MacDonald, Ingelfinger, and Belding (1947) found that the condition had developed in about 44 per cent of patients who had survived three or more years after operation and who had had no prophylactic therapy. Several recent reports suggest that the incidence may be higher still and that it increases with the passage of time.

A similar condition sometimes follows gastro-enterostomy and partial gastrectomy, but there is no evidence that its incidence after these procedures is any higher than it is in the general population.

We describe here 10 cases of megaloblastic anæmia following gastrectomy. In 5 the resection had been total or near-total. There were no complicating factors and in each absence of the stomach was the probable cause of the anæmia. In the other 5 cases the resection had been partial. In all of these there were either other gastro-intestinal lesions or serious dietary deficiencies which probably caused or contributed to the development of the anæmia. Peripheral macrocytosis and intermediate megaloblasts in the bone-marrow were sometimes found before the condition had fully developed. Seven cases were treated with vitamin B_{12} and different responses to it are described.

CASE REPORTS

(*Tables I, II.*)

CASES FOLLOWING TOTAL GASTRECTOMY*

Case 1.—H. T. E., male, aged 35. Near-total gastrectomy (gastrojejunal anastomosis) in 1945 for a high simple gastric ulcer. Before operation, gastric secretion and peripheral blood were normal.

In September, 1950, there were various complaints, including œdema, loss of energy, and loss of weight. He was pale but had no glossitis or nervous lesion. His diet was adequate. The hæmoglobin was 10·1 g./100 ml., erythrocytes 3·0 × 10^6 per c.mm., M.C.V. 110 cu. microns. The peripheral blood-smear showed macrocytosis and megaloblasts. The bone-marrow was not examined. He was treated with parenteral liver extract, 2 ml. daily for two weeks, on alternate days for a further two weeks, and weekly thereafter. After four weeks the blood was almost normal (Hb 16·3 g./100 ml.). No reticulocyte counts were made. The patient regained his energy and his colour improved. A barium meal showed no abnormality in the intestines. A three-day fat intake-excretion test showed 74 per cent absorption. (Unfortunately we did not see this patient until treatment had been started and were therefore unable to investigate him thoroughly, but there can be little doubt about the diagnosis.)

Case 2.—G. H. G., male, aged 62. Near-total gastrectomy (gastrojejunal anastomosis) in December, 1946, with removal of spleen, half the pancreas, and a portion of the transverse colon for an extensive infiltrating carcinoma of the stomach. No pre-operative test-meal or blood examination was made. His first cousin had Addisonian pernicious anæmia.

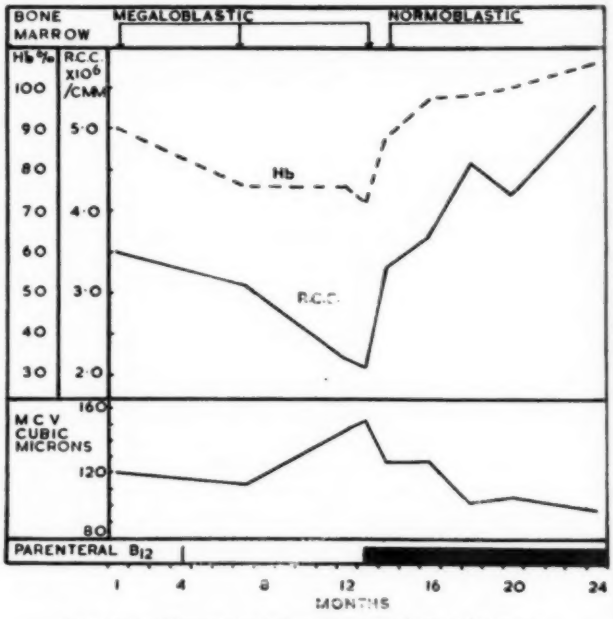

FIG. 508.—Hæmatological response to therapy in *Case* 2.

In March, 1948, moderate macrocytosis was found in the peripheral blood and this was more marked a year later. In April, 1950, the hæmoglobin was 13·3 g./100 ml., erythrocytes 3·5 × 10^6 per c.mm., M.C.V. 120 cu. microns, and intermediate megaloblasts were present in the bone-marrow.

In April, 1951, he complained of breathlessness on exertion, swelling of the ankles, and a sore tongue. There were no neurological signs. His diet was adequate and a three-day fat intake-excretion test showed 56 per cent absorption. Hæmoglobin 10·5 g./100 ml., erythrocytes 2·1 × 10^6 per c.mm., M.C.V. 152 cu. microns, and the bone-marrow frankly megaloblastic.

Treatment was commenced with parenteral vitamin B_{12}, 100 μg. daily for two days, then 40 μg. weekly. A maximum reticulocyte crisis of 16·5 per cent occurred on the eleventh day (calculated optimum 13 per cent) and the marrow became normoblastic four days after the start of treatment. Clinical improvement followed and all the

* In *Cases* 1 and 2 a ½-in. fringe of stomach was left at the cardiac end to facilitate the anastomosis.

symptoms and signs disappeared in a few weeks. The peripheral macrocytosis, however, persisted for some time and the blood-picture was not entirely normal until between seven and eleven months after starting parenteral treatment. (*Fig.* 508.)

In November, 1953, the patient suffered an intercurrent attack of pneumonia, following which parenteral B_{12} therapy was discontinued and oral B_{12} treatment substituted. On this treatment the clinical and hæmatological improvement has been maintained. When last seen in September, 1954, the hæmoglobin was 17·3 g./100 ml., erythrocytes 5·9 × 10^6 per c.mm., and the M.C.V. 86 cu. microns.

Case 3.—J. G., male, aged 40. Total gastrectomy (œsophagojejunal anastomosis) in 1947 for carcinoma of the stomach. Before operation he was achlorhydric and had slight hypochromic anæmia. He remained well until 1953, when he complained of loss of weight, anorexia, and lassitude. He was very pale and had superficial glossitis. His diet was adequate. In August, 1953, the hæmoglobin was 11·7 g./100 ml., erythrocytes 2·28 × 10^6 per c.mm., leucocytes 5900 per c.mm., reticulocytes less than 0·5 per cent, M.C.V. 136 cu. microns. The peripheral blood-film showed poikilocytosis, anisocytosis, macrocytosis, and occasional nucleated red cells. The neutrophils were large and multilobed. The bone-marrow showed a megaloblastic erythropoiesis.

He was treated with vitamin B_{12} parenterally, 50 μg. daily for 12 days, followed by 50 μg. weekly for three months. The maximum reticulocyte response obtained was 8·5 per cent (calculated optimum 11·3 per cent) and the average weekly red-cell rise during the first two weeks of therapy was 0·365 × 10^6 per c.mm. (calculated optimum of 0·453 × 10^6 per c.mm.). The hæmoglobin was restored to normal (16·6 g./100 ml.) within three months (*Fig.* 509) but the erythrocyte count was much slower in

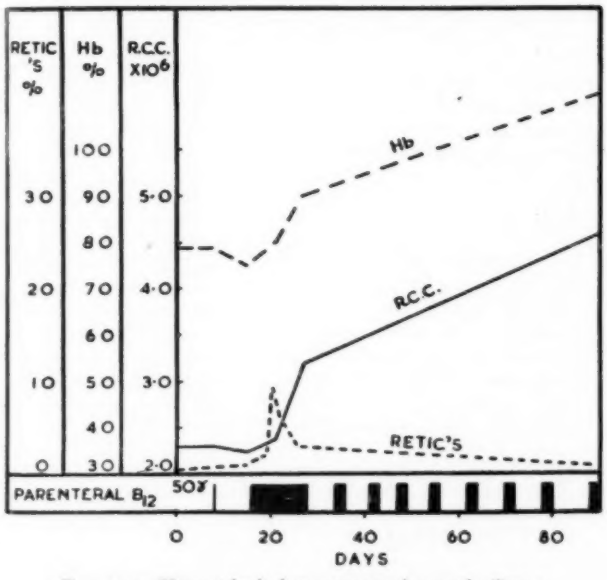

FIG. 509.—Hæmatological response to therapy in *Case* 3.

its response so that the macrocytosis persisted and even after three months' treatment the M.C.V. was still 100 cu. microns.

Case 4.—R. M., female, aged 32. Total gastrectomy (œsophagojejunal anastomosis) in March, 1949, with removal of spleen and tail of pancreas for an extensive carcinoma of the stomach. Before operation she was achlorhydric and had a mild hypochromic anæmia. In 1950 her tongue was smooth and a year later it became sore. At this time she suffered from diarrhœa and developed œdema of the ankles and sacral area. Plasma-proteins were 6·1 g./100 ml. She improved on a high-protein intake and her diet remained adequate. In February, 1953, she had a high colour index and in

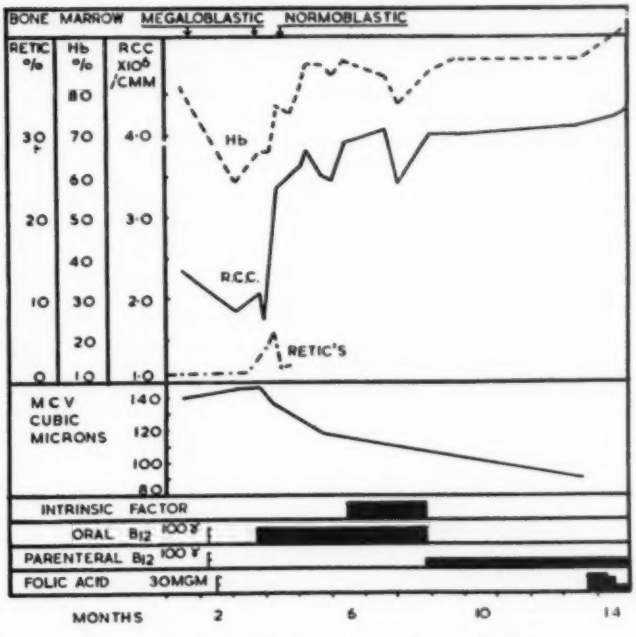

FIG. 510.—Hæmatological response to therapy in *Case* 4.

August marked macrocytosis. In September the marrow contained intermediate megaloblasts and the tongue was smooth, red, and very sore. Riboflavin, 10 mg. t.d.s. by mouth, produced marked improvememnt in the tongue. In November the hæmoglobin was 8·7 g./100 ml., erythrocytes 1·85 × 10^6 per c.mm., and the M.C.V. 144 cu. microns. The marrow was typically megaloblastic and treatment with vitamin B_{12} *by mouth*, 100 μg. daily, was started. A reticulocyte crisis of 6 per cent (calculated optimum 17 per cent) occurred on the eleventh day, and the blood-picture improved steadily for two months, thereafter becoming stationary, with the hæmoglobin fixed at a suboptimal level. Despite this, clinical improvement was marked and all the symptoms and signs disappeared. In February, 1954, intrinsic factor as well as vitamin B_{12} was given by mouth and continued for three months. The hæmoglobin and erythrocyte count were maintained but did not improve. Parenteral B_{12} therapy was then started, 50 μg. being given weekly at first, and later every two weeks, but this did not produce any further improvement in the hæmoglobin or erythrocyte levels. The addition of oral folic acid supplement to the parenteral vitamin B_{12} treatment resulted in rapid improvement and the hæmoglobin rose in one month from 12·5 to 14·0 g./100 ml. (*Fig.* 510).

Case 5.—J. C., male, aged 60. Total gastrectomy (œsophagojejunal anastomosis) with removal of spleen and half the pancreas in April, 1950, for a high simple gastric ulcer thought to be malignant at operation. Before operation the peripheral blood was normal. During the next two years he failed to gain weight, suffered from diarrhœa, and developed œdema of the ankles and a mild normochromic anæmia. His diet was adequate. By July, 1953, the anæmia, though still slight (hæmoglobin 11·8 g./100 ml.) was frankly macrocytic and the M.C.V. was 120 cu. microns. Treatment was withheld and the patient kept under review for eight months, during which time there was very little change in the blood-picture. In April, 1954, the hæmoglobin was 11·3 g./100 ml., erythrocytes 2·98 × 10^6 per c.mm., leucocytes 3900 per

c.mm., reticulocytes 0·8 per cent, M.C.V. 120 cu. microns, serum-bilirubin 0·23 mg./100 ml. The blood-film showed macrocytosis and minimal anisocytosis. He had a burning feeling in his feet and a general weakness in his legs. No neurological changes suggestive of cord degeneration could be elicited on clinical examination. This clinical condition failed to respond to massive oral doses of thiamine. In April, 1954, the bone-marrow showed a mixed type of erythropoiesis and the presence of numerous intermediate megaloblasts.

Parenteral vitamin B_{12} therapy consisting of 50 μg. weekly was then commenced and continued for three months. The general condition of the patient then rapidly improved; he ate more, gained weight, and lost the paræsthesiæ and weakness in the lower limbs. The erythrocyte count mounted from $2·75 \times 10^6$ to $3·62 \times 10^6$ per c.mm., the M.C.V. fell to normal range, but the hæmoglobin level remained unaffected.

A change to parenteral liver extract, later combined with oral folic acid, failed to produce any further rise in the hæmoglobin level, which remained suboptimal. The addition of oral ferrous gluconate to the latter therapy resulted in a rapid restoration of the hæmatological picture to normal. When last seen in January, 1955, the hæmoglobin was 15·5 g./100 ml., erythrocytes $4·60 \times 10^6$ per c.mm., and M.C.V. 98 cu. microns.

Cases following Partial Gastrectomy

Case 6.—G. R., female, aged 53. Partial (75 per cent) gastrectomy (gastrojejunal anastomosis) in October, 1947. She had a previous history of duodenal ulcer which in 1943 was followed by stenosis, vomiting, great loss of weight, vitamin deficiency, and severe hypochromic anæmia which responded to blood transfusions and iron. By 1946 her gastric mucosa had become atrophic as judged by gastroscopy and she had a histamine-fast achlorhydria. She underwent exploratory laparotomy, gastro-enterostomy, and entero-anastomosis, but continued to vomit and suffer abdominal pain. At gastrectomy in 1947 no signs of active ulceration were found. After operation she ate very little but took milk and red meat occasionally. A barium meal showed a deficiency pattern in the small intestine and fat absorption was 70 per cent.

In 1948 the hæmoglobin was 11·2 g./100 ml., erythrocytes $2·5 \times 10^6$ per c.mm., and she had developed a megaloblastic erythropoiesis in the bone-marrow. The anæmia responded to parenteral liver extract therapy, 2 ml. weekly. She underwent two further operations for chronic obstruction and her nutritional troubles increased.

(This case was described in more detail by Welbourn, Hughes, and Wells (1951).)

Case 7.—J. B., female, aged 57. Partial (about 50 per cent) gastrectomy (gastrojejunal anastomosis) in 1939 for peptic ulcer. There is no record of a blood examination or test-meal before operation. About 1946 she noticed weakness, dyspnœa, loss of weight, and soreness of the tongue. In February, 1949, her blood showed macrocytosis and she was given liver injections by her doctor. In June, 1950, the liver was stopped and she was investigated fully. She had superficial glossitis and angular stomatitis. Her diet was very restricted, consisting of tea, white bread and butter, tea with milk, and occasional tripe. A fractional test-meal showed a histamine-fast achlorhydria. A barium meal was normal. There was mild iron-deficiency anæmia, which was treated with intravenous iron, but within two months the blood again became macrocytic and the marrow megaloblastic. At this time the hæmoglobin was 12·7 g./100 ml., erythrocytes $3·5 \times 10^6$ per c.mm., M.C.V. 117 cu. microns. She was treated with vitamin B_{12} intramuscularly, 100 μg. daily for one week, followed by 40 μg. weekly. The marrow was normoblastic four days later and a maximum reticulocyte response of 6·0 per cent occurred on the seventh day (calculated optimum 0·8 per cent). Although the hæmoglobin concentration rose steadily, there was no fall in the M.C.V. after eight weeks' treatment. It became difficult to keep in touch with the patient and folic acid 20 mg./day by mouth and liver, 1 ml. about every two weeks intramuscularly, were given, instead of vitamin B_{12}. The M.C.V. then fell steadily and was normal in four months. The tongue and lip lesions did not respond to this treatment nor to vitamin B complex. Some months later the patient died from unrelated causes.

Case 8.—J. S., male, aged 69. Partial (about 50 per cent) gastrectomy (gastroduodenal anastomosis) in 1948 for benign gastric ulcer. Pre-operatively there were multiple diverticula of the small intestine and clinical steatorrhœa. No test-meal or blood examination was made. By 1951 he had developed severe nutritional disorders, including loss of weight, gross œdema, and hypoproteinæmia. Fat absorption was 78 per cent. Fractional test-meal showed histamine-fast achlorhydria. His diet was adequate. The blood was hyperchromic and the marrow contained intermediate megaloblasts. He was treated with oral folic acid and parenteral liver extract, but no further hæmatological investigations were possible.

Case 9.—J. D. S., male, aged 37. Following a forceps injury at birth he was mentally defective, suffered from epileptic fits, and had a right hemiplegia. In 1952 he had a hæmatemesis, and radiological examination revealed the presence of a duodenal ulcer. Examination of the blood showed a moderate normocytic anæmia. Further severe intestinal hæmorrhages occurred and in February, 1953, an emergency partial (60–70 per cent) gastrectomy (gastrojejunal anastomosis) was carried out. Immediately before operation he was gastroscoped and the gastric mucosa appeared atrophic. On section it was normal in structure and thickness.

After operation his diet was very restricted, consisting of bread and butter and tea and an occasional egg. By February, 1954, he had lost over 100 lb. in weight and had become severely anæmic. Hæmoglobin 3·1 g./100 ml., erythrocytes $0·65 \times 10^6$ per c.mm., leucocytes 6800 per c.mm., reticulocytes less than 0·5 per cent, colour index 1·57, M.C.V. 138 cu. microns. Differential leucocyte count normal. Stained film showed anisocytosis, poikilocytosis, and macrocytosis. Serum-bilirubin 1·2 mg./100 ml. The bone-marrow showed a megaloblastic type of erythropoiesis. A transfusion with four pints of packed cells was given. This was followed by adequate parenteral B_{12} therapy to which response was poor and the maximum reticulocyte rise was 6·5 per cent (calculated optimum 48 per cent). The presence of a bronchopneumonia unresponsive to antibiotic therapy may have been responsible for the lack of response. The patient died some four weeks after admission to hospital of bilateral bronchopneumonia with abscess formation.

At autopsy the bilateral bronchopneumonia was confirmed and the presence of a left cerebral atrophy with cyst formation detected. The bone-marrow was actively hæmopoietic throughout the skeleton.

Case 10.—H. K., male, aged 44. Partial (75 per cent) gastrectomy (gastrojejunal anastomosis) in November, 1951, for a carcinoma of the pyloric antrum. The blood was normal prior to operation (hæmoglobin 16·1 g./100 ml.). For two years after operation he remained weak and tired easily. He suffered from anorexia, ate very little, and lost weight. In November, 1953, he was readmitted with acute retention of urine which was relieved by catheterization. He was semicomatose, listless, unresponsive, and pale. Examination of the blood revealed a macrocytic anæmia. Hæmoglobin 6·3 g./100 ml., erythrocytes $1·88 \times 10^6$ per c.mm., leucocytes 1850 per c.mm., M.C.V. 100 cu. microns,

serum-bilirubin 0·4 mg./100 ml. The bone-marrow showed active megaloblastic erythropoiesis. Parenteral vitamin B_{12} therapy was commenced and the patient received 1·45 mg. in 50 days. (*Fig.* 511.) The maximum reticulocyte response of 19·5 per cent was better than the

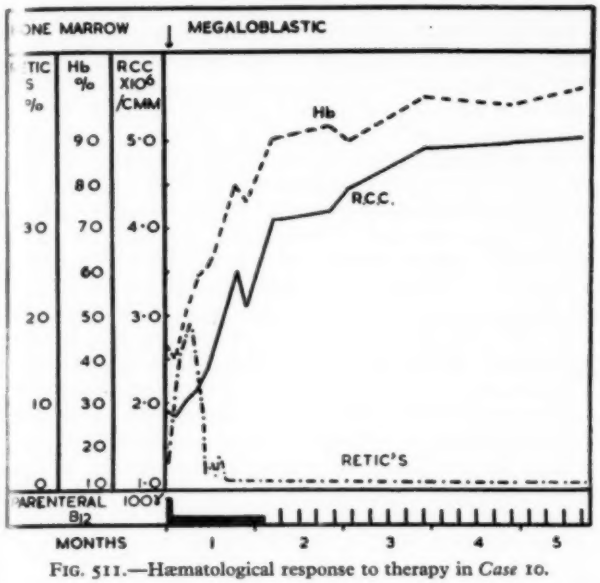

FIG. 511.—Hæmatological response to therapy in *Case* 10.

calculated optimum of 16 per cent. After maintenance with B_{12} therapy for three months the blood had been restored to normal (hæmoglobin 14·8 g./100 ml., erythrocytes $4·9 \times 10^6$ per c.mm.). The general condition of the patient had greatly improved and weight gain of 15 lb. had been achieved.

COMMENTARY

Megaloblastic Anæmia following Partial Gastrectomy.—From a study of the literature it would appear that post-operative megaloblastic anæmia occurs in only a very small proportion of cases following partial gastrectomy. Berg (1930), Hartfall (1934), Lake (1937), and Pulvertaft (1952) found no cases in their comparatively large series. One of us (Welbourn, 1953) found none in a continuous series of 253 cases of partial gastrectomy undertaken for peptic ulcer. Lyngar (1950) examined the bone-marrows in a series of 146 patients, and found inhibition of maturation, but no evidence of megaloblastosis. Individual case reports of megaloblastic anæmia following partial gastrectomy have been recorded (Rowlands and Simpson, 1932; Rhodes and Grunberg, 1943; Morgans, Rimmington, and Whittaker, 1947; Larsen, 1952, Gouttas, 1953; Naish and Capper, 1953). In our 5 cases the anæmia appeared from one to ten years after partial gastrectomy. In none was it possible to incriminate the gastric resection as the sole, or even the main, cause of the anæmia. In 2 there were factors present *before* operation which might well have caused a megaloblastic anæmia. One (*Case* 6) had histamine-fast achlorhydria and another (*Case* 8) multiple diverticula of the small intestine and steatorrhœa. The other three (*Cases* 7, 9, and 10), although *able* to eat adequately, in fact consumed diets which were grossly deficient in hæmopoietic factors.

Table I.—SUMMARY OF CLINICAL DETAILS IN 10 CASES

CASE NO.	SEX	AGE	GASTRIC LESION	OPERATION	POST-OPERATIVE PERIOD
1	M.	35	Gastric ulcer	Total gastrectomy	5 yr.
2	M.	62	Gastric carcinoma	Total gastrectomy	5 yr.
3	M.	40	Gastric carcinoma	Total gastrectomy	6 yr.
4	F.	32	Gastric carcinoma	Total gastrectomy	4 yr.
5	M.	60	Gastric ulcer	Total gastrectomy	4 yr.
6	F.	53	Duodenal ulcer	Partial gastrectomy	1 yr.
7	F.	57	Peptic ulcer	Partial gastrectomy	10 yr.
8	M.	69	Gastric ulcer	Partial gastrectomy	3 yr.
9	M.	37	Duodenal ulcer	Partial gastrectomy	1 yr.
10	M.	44	Gastric carcinoma	Partial gastrectomy	2 yr.

Table II.—SUMMARY OF HÆMATOLOGICAL FINDINGS IN 10 CASES

CASE NO.	HB G./100 ML.	R.C.C. MILLION/CU. MM.	M.C.V. CU. MICRONS	BONE-MARROW
1	10·1	3·0	110	Not examined
2	10·5	2·1	152	Megaloblastic
3	11·7	2·28	136	Megaloblastic
4	8·7	1·85	144	Megaloblastic
5	11·3	2·98	120	Megaloblastic
6	11·2	2·50	—	Megaloblastic
7	12·7	3·5	117	Megaloblastic
8	14·1	3·9	—	Megaloblastic
9	3·1	1·57	138	Megaloblastic
10	6·3	1·88	100	Megaloblastic

Megaloblastic Anæmia following Total or Near-total Gastrectomy.—Megaloblastic anæmia was found in all the 5 cases which we have personally studied for a period of four years or more after total gastrectomy and which have had no prophylactic therapy. Three of these (*Cases* 2, 4, and 5) were found in two series of cases which we followed deliberately (*Table III*) and represent all the patients who survived for four or more years. The other two (*Cases* 1 and 3) were operated on elsewhere and were referred to us when they had developed anæmia.

Table III.—INCIDENCE OF MEGALOBLASTIC ANÆMIA AT YEARLY INTERVALS AFTER TOTAL OR NEAR-TOTAL GASTRECTOMY

Years after Operation	*No. of Patients Surviving*	*No. having Megaloblastic Anæmia*
1	6	0
2	4	0
3	4	2
4	3	3

Two series of cases (from the surgical professional units at the Liverpool Royal Infirmary and the Royal Victoria Hospital, Belfast) have been combined. Patients who received prophylactic therapy have been excluded. The two other cases of megaloblastic anæmia which are reported (Nos. 1 and 3) were operated on elsewhere.

This incidence agrees with that of 6 out of 10 reported by Blake and Rechnitzer (1953) and 8 out of 8 reported by Fellinger (1950). In our 5 cases the interval between the operation and the appearance of macrocytic anæmia varied from one to six years. MacDonald and others (1947) considered that macrocytic anæmia rarely developed within two years after gastrectomy, although it was common if the patient lived three years or more. Indeed Fellinger (1950) described megaloblastic anæmia in every one of eight patients who survived from five to eight years. These findings tend to support the view of Bethell, Sturgis, Rundles, and Meyers (1945) that megaloblastic anæmia will always follow a total gastrectomy provided the patient lives long enough after operation and receives no prophylactic treatment. With modern pre-operative preparation, surgical technique, and post-operative management it is likely that survival will be prolonged and consequently the problem of post-operative megaloblastic anæmia will loom large in the long-term management of these cases in the future.

In none of our cases were there complicating aetiological factors such as there were in those following partial gastrectomy. In particular all were eating adequate diets. Two (*Cases* 3 and 4) are known to have been achlorhydric before operation, and it might be argued that they would have developed a megaloblastic anæmia without gastric resection. However, the anæmia which accompanies gastric carcinoma and that which follows *partial* gastrectomy for carcinoma is usually hypochromic and microcytic in type, and in two of our cases (*Cases* 1 and 5), as well as in some in the literature, the megaloblastic anæmia followed resection for benign lesions. It is difficult to avoid the conclusion that it is very extensive gastric resection which is directly responsible for the change in hæmopoiesis. It is of interest that two of the cases (*Cases* 1 and 2) did not have strictly total resections. The very small fringe of stomach which was left was, however, very much smaller than that which is usually left after a high subtotal resection for duodenal ulcer. In other respects, such as loss of weight and impaired absorption of fat, these two cases behaved like *total* and not like subtotal gastrectomies, and it is clear that ½ in. of the cardiac end of the stomach is functionally insignificant.

Clinical Features.—Characteristically post-gastrectomy megaloblastic anæmia has a gradual onset, and when the condition is fully established the symptoms resemble true Addisonian pernicious anæmia. In some cases the glossitis is severe and associated with angular stomatitis, and may be aggravated by riboflavin deficiency. The presence of cord changes has been described in post-gastrectomy megaloblastic anæmia by Dennig (1929), Meyer, Schwarz, and Weissman (1941), MacDonald and others (1947), Beebe and Meneely (1949). The appearance of tingling in the feet and some unsteadiness of gait was noted in one of our cases (*Case* 5). Vibration sense was unimpaired and no other signs of cord changes could be elicited.

Early Hæmatological Changes.—In many of our cases we were able to demonstrate the appearance of macrocytosis before the onset of frank anæmia (*Fig.* 508). For this reason we believe that the presence of a relatively high hæmoglobin level with a macrocytic peripheral blood-picture is the earliest sign indicating the development of a post-gastrectomy megaloblastic anæmia. During the follow-up study of some of our cases a slow but steady fall in the hæmoglobin was noted. However, even though the hæmoglobin was 11–12 g./100 ml., the red-cell count had fallen to $3{\cdot}0 \times 10^6$ or less and the M.C.V. had risen to 120 cu. microns or greater. The demonstration of a megaloblastic marrow in all but one instance confirmed the presence of a deficiency of anti-megaloblastic substances and the need for therapy. Treatment in some cases was withheld and repeated bone-marrow examinations were made. Under these circumstances it was possible to see the evolution and progression of the megaloblastosis of the marrow. The early changes consisted of a relative preponderance of more primitive erythropoietic cells and the appearance of macro forms with a nuclear structure intermediate between normoblasts and megaloblasts. As such cells appear in the bone-marrow in states associated with minor deficiency of antimegaloblastic substances they probably have the same pathogenesis as true megaloblasts. Their morphological differentiation from true megaloblasts is a question of degree rather than of kind and in accordance with accepted usage the term intermediate megaloblast has been used throughout to describe these cells.

Response to Therapy.—The response of post-gastrectomy megaloblastic anæmia to treatment with parenteral liver extract or vitamin B_{12} is on the whole similar to that of Addisonian pernicious anæmia. With adequate therapy, a reticulocyte crisis occurs and normal values for the hæmoglobin and red-cell count are usually obtained in three months (*Figs.* 509, 511). The rapid conversion by specific treatment of the megaloblastic change in the marrow to normoblastic has been demonstrated in a few instances (*Figs.* 508, 510).

With the exception of cases reported by Fellinger (1950) all the other reported cases which were treated with liver preparations responded in the usual way. Fellinger's patients were refractory to liver, but responded well to meat mixed with normal gastric juice by mouth. Parenteral liver extract produced an entirely satisfactory response in two cases in this series (*Table IV*).

An excellent clinical and hæmatological response was obtained in 4 of 7 patients who received parenteral B_{12} therapy alone (*Table V*). One case (*Case* 9) which failed to respond was complicated by an antibiotic-resistant bronchopneumonia which proved fatal shortly after therapy had started. In another case (*Case* 5) the clinical response to vitamin B_{12} was good, but no significant change occurred in the hæmoglobin level on parenteral vitamin B_{12} treatment. A change to parenteral liver extract later combined with oral folic acid failed to produce further hæmatological improvement, but when oral iron was added then the hæmoglobin level rose rapidly to normal.

Although oral folic acid has produced remissions in some cases (Bethell, Meyers, Andrews, Swendseid, Bird, and Brown 1947; Zollinger and Finch, 1947; Morgans and others, 1947; Ariyoshi, 1951), it cannot be regarded as safe treatment because of the

well-established inability of folic acid to prevent the neurological complications in Addisonian pernicious anæmia. However, the addition of folic acid to supplement parenteral vitamin B_{12} and liver extract therapy has been found to have advantages and to convert an otherwise suboptimal hæmatological response into an entirely satisfactory one (MacDonald and others, 1947; Conway and Conway, 1951; Ariyoshi, 1951, Beyers, Diefenbach, Mark, and Meyer, 1952; Larsen, 1952, and in *Case* 4 of this series).

The necessity for folic acid supplement to liver extract or parenteral vitamin B_{12} therapy in some cases of post-gastrectomy megaloblastic anæmia conforms with the generally accepted view that for efficient hæmopoietic action the presence of adequate amounts of vitamin B_{12}, folic acid, and ascorbic acid are essential. It is probable that if any one of these substances is markedly deficient the administration of any of the other anti-megaloblastic substances will not produce a complete cure. After gastrectomy there is likely to be a deficiency of folic acid because of the intestinal dysfunction associated with the agastric state, and there is therefore much to be said for the use of combined B_{12} and folic acid therapy in these cases.

Table IV.—EFFECT OF TREATMENT WITH PARENTERAL LIVER EXTRACT IN 3 CASES

CASE NO.	DURATION OF TREATMENT MONTHS	GENERAL RESPONSE	HB AFTER TREATMENT G./100 ML.	COMMENT
1	2	Good	16·3	—
6	6	Good	13·0	Persistent macrocytosis
8	—	Not known	—	—

One patient with megaloblastic anæmia after total gastrectomy (*Case* 4) received 100 μg. of vitamin B_{12} daily *by mouth* for a period of three months. This treatment produced a reticulocyte response lower than the calculated optimum, and a rise in the red-cell count which became fixed at a suboptimal level despite maintained therapy (*Fig.* 510). The fact that any response occurred during oral administration of vitamin B_{12} in an agastric patient requires some explanation. It is believed that total gastrectomy removes the major part, if not the whole, of the area of the intestine which elaborates intrinsic factor. The absence of intrinsic factor, so produced, would render any ingested vitamin B_{12} biologically unavailable. Consequently, oral vitamin B_{12} treatment should theoretically have been therapeutically ineffective. The recent work of Callender, Turnbull, and Wakisaka (1954) on the absorption of radio-active vitamin B_{12} has shed some light on this problem. These workers have shown that, after total gastrectomy, the majority of subjects show poor absorption of vitamin B_{12} and the degree of absorption resembles that already described in cases of Addisonian pernicious anæmia. However, occasional cases show a moderate absorption of vitamin B_{12} after gastrectomy, indicating possibly the continued excretion of intrinsic factor either from an incompletely resected stomach or from some extragastric source (such as ectopic gastric mucosa). The response to oral vitamin B_{12} therapy in our case (in whom the stomach had been completely resected) suggests an extragastric source of intrinsic factor. A change from oral to parenteral vitamin B_{12} therapy in *Case* 4 did not result in any further improvement in the hæmoglobin level, which remained fixed in the region of 12·0 g./100 ml. Suboptimal responses with parenteral vitamin B_{12} have been recorded by Conway and Conway (1951), Ariyoshi (1951), and Larsen (1952). It is interesting to note that in this case the blood-picture was not finally restored to normal until both parenteral vitamin B_{12} and oral folic acid therapy were used (*Fig.* 510).

Table V.—EFFECT OF TREATMENT WITH PARENTERAL VITAMIN B_{12} IN 7 CASES

CASE NO.	DURATION OF TREATMENT MONTHS	GENERAL RESPONSE	HB AFTER TREATMENT G./100 ML.	COMMENT
2	3	Good	14·4	Persistent macrocytosis
3	3	Excellent	16·6	—
4	3 1	Good Good	13·0 14·5	+ oral folic acid
5	2	Fair	9·6	Later Hb rose to 15·5 g. on combined liver extract, oral folic acid and iron
7	3	Good	14·9	Persistent macrocytosis
9	1	Poor	7·8	Died
10	3	Excellent	13·3	—

Delayed onset of Megaloblastosis.—The long delay in the development of the anæmia after total gastrectomy can be explained by the fact that the body stores of B_{12} have been adequate prior to the operation. Girdwood (1952) has shown that the normal daily requirements of B_{12} approximate to 1 μg. a day and the body stores are of the order of 1000–2000 μg. Consequently, three to six years would be required to exhaust the stores completely and for a deficiency of this antimegaloblastic substance to become manifest.

Hæmatological Management following Total Gastrectomy.—There is a need for careful hæmatological studies during the follow-up of patients who have been subjected to total gastrectomy. This is dictated by the frequency with which megaloblastic anæmia occurs among patients who survive three years or longer. The development of a similar complication following partial gastrectomy is relatively uncommon but should not be neglected. The macrocytic anæmia may develop gradually over a number of years. This does not mean that relapse may not occur more rapidly. In Addisonian pernicious anæmia the speed of development of relapse is exceedingly variable, and it is likely that the same applies to post-gastrectomy megaloblastic anæmia; cases may present with a sudden onset. If the condition remains untreated not only will the anæmia become more severe but

cord changes may possibly develop. Consequently a careful post-operative follow-up study should be made in these patients. The hæmoglobin estimation alone is not reliable in the early detection of post-gastrectomy megaloblastic anæmia, because relatively high levels are often found in the early stages, and it is necessary to carry out a more detailed examination of the peripheral blood than is usual in surgical follow-up clinics. Not only should the hæmoglobin be determined but a peripheral blood-smear should be examined for the presence of macrocytosis. If this is found, the M.C.V. should be determined and the bone-marrow examined. Once a megaloblastic anæmia has developed after total gastrectomy, treatment with liver extract, parenteral B_{12}, or a combination of these drugs with oral folic acid, and oral iron, has proved adequate to restore the blood-picture to normal. Nevertheless, there is much evidence to support the routine use of preventive therapy, especially in view of the frequency of this complication. As suggested by Callender and others (1954) the prophylactic administration of vitamin B_{12} parenterally to all patients after total gastrectomy is indicated. This is particularly important for all those patients who do not remain under strict medical supervision.

SUMMARY

1. The literature on post-gastrectomy megaloblastic anæmia is briefly reviewed.

2. Ten further cases of our own are presented, five of which followed total or near-total and five partial gastrectomy.

3. In all those following partial gastrectomy there were other gastro-intestinal lesions or serious dietary deficiencies which probably caused or contributed to the development of the anæmia.

4. The importance of peripheral macrocytosis in the absence of significant anæmia is stressed as an early sign of the development of megaloblastic anæmia after gastrectomy. This is accompanied by changes in the bone-marrow consisting of a relative preponderance of more primitive erythroblasts and the appearance of early intermediate megaloblasts.

5. There is need for careful hæmatological studies in the follow-up of post-gastrectomy patients, particularly when the gastrectomy is total.

6. The response to parenteral vitamin B_{12} was extremely satisfactory in four of seven patients. Of the other three cases, one died of intercurrent infection, the second required the addition of oral folic acid supplement to obtain optimal response, and the third did not improve on change of therapy to parenteral liver, later combined with oral folic acid. In this last case the addition of oral iron to this combined therapy was needed to restore the blood-picture.

7. The response obtained with oral vitamin B_{12} therapy in one case is discussed.

8. Our studies indicate the need for prophylactic treatment with parenteral vitamin B_{12} of all patients who have had a total or near-total gastrectomy.

We wish to thank the various physicians and surgeons who referred cases to us, particularly Professor Harold Rodgers and Professor Charles Wells, under whose care many of the patients were admitted. We are indebted to Mr. A. Lamont, F.I.M.L.T., for preparing the graphs.

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EXPERIMENTAL SURGERY

THE RESISTANCE TO DIGESTION OF THE STOMACH-IMPLANTED DOG'S COLON*

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THE use of colon loops to replace resected portions of stomach was introduced by Moroney (1951, 1953) in the treatment of peptic ulcers in man. The rationale for this procedure lay in his single observation that a portion of colon necessarily left behind in communication with the gastric lumen in the preliminary repair of a gastrocolic fistula was at subsequent operation found to be intact and undigested.

This experience had been recorded before by Wilkie (1934) in a case of gastrocolic fistula, and by Eggers (1939) in a case of gastrojejunocolic fistula.

There is no record of an experimental investigation into the use of colonic loops for this purpose. Previous studies on the resistance of the intestine to peptic digestion have been made, but provided inconsistent results. The implantation of loops of small intestine into the stomach lumen of animals was first carried out in 1908 by Katzenstein, and in the same year by Kathe. Both workers found that the implanted loops were rapidly digested. Hotz (1910) and Licini (1912) repeated the study and claimed that digestion did not occur if the blood-supply to the loop was carefully preserved, but this was denied by Best (1914) as the result of a further study on cats in which he used implants of both jejunum and colon.

Fiori (1913) transected the pyloric antrum and restored alimentary continuity with a segment of jejunum. The three dogs used survived 5, 22, and 43 days, during which no digestive effect on the implant was observed. The author did not state whether the animals were sacrificed or why they died.

Patches of jejunum were implanted into the wall of the antrum of dogs by Mann (1916), and it was shown that the patches resisted digestion even when necrosis and ulcers occurred in the rest of the stomach in response to subsequent bilateral adrenalectomy. Dragstedt and Vaughan (1924) cut a window out of the anterior wall of the lower third of the stomach in three dogs and filled it with a flap fashioned from a loop of intestine "including colon", preserving the original blood-supply. These dogs were sacrificed after "1 to 12 months" and in no case had any digestion of the intestinal flaps occurred. In a second group of three dogs the window was filled by the serosal surface of an unopened loop of "intestine", and when sacrificed one or two months later complete ulceration had occurred in the part of the intestine exposed to the gastric juice. Reerink (1950) similarly reported that patches of colon implanted into the stomach wall did not ulcerate.

Such reports suffer from lack of adequate data, and the failure to make allowance for physical factors in the experimental production of peptic ulcer.

Thus Price and Lee (1946) demonstrated that when an organ was implanted tangentially into the stomach wall, digestion of its surface did not occur, but when allowed to project into the lumen of the stomach digestion occurred until the ulcerated surface was level with the surrounding gastric mucosa. Saltzstein and Kurtz (1946) placed jejunal patch implants into the stomach of dogs in which the duodenum had previously been by-passed by the gastro-enterostomy technique described by Mann and Williamson (1923). Whereas the jejunum distal to the gastro-enterostomy stoma consistently ulcerated, the implant in the nearby gastric wall remained intact.

The object of the present study was to examine the resistance of the dog's colon to peptic digestion when placed in continuity with the stomach and duodenum and thus subject to mechanical and motility stresses, as well as to gastric juice activity, as is the human colon in Moroney's operation of replacement of the stomach. It was also intended to compare the resistance of the implanted colon with that of the stomach and duodenum to the effects of continuous stimulation by means of daily injections of histamine-in-beeswax (Hay, Varco, Code, and Wangensteen, 1942).

EXPERIMENTAL METHOD

Eleven dogs were used, with an average weight of 20 kg.

Oral phthalylsulphathiazole was administered for three days prior to operation to reduce the bacterial flora of the intestine. The fasting dog was anæsthetized with intravenous nembutal followed by a mixture of ether and air through an endotracheal tube. A loop of colon 3–4 in. long, in site corresponding to the human transverse colon, was resected between non-traumatic clamps, care being taken to preserve the blood-supply. The colon continuity was restored by end-to-end anastomosis anterior to the pedicle of the resected loop (*Fig.* 512 A, B). In order to determine if the continuity of the direction of peristalsis in the stomach and the colon was essential to satisfactory functioning of the implant as a replacement for the resected part of the stomach, in the last two groups of dogs the loop was implanted in antiperistaltic fashion. The operation

* This study was carried out during the term of a Clinical Research Fellowship of the Endowments Fund of the Sheffield United Hospitals.

then proceeded in one of the following three ways :

Group 1.—In 6 dogs the stomach was transected at the junction of the antrum with the body, and after suitably reducing the lumen of the ends of the two gastric segments, the free loop of colon was anastomosed to them isoperistaltically (*Fig.* 512 C). Six dogs were thus prepared.

Three dogs were thus prepared, but leakage occurred from the proximal gastrocolonic suture line in two, which had to be destroyed. The third dog remained well until sacrificed after fourteen weeks.

The implant was placed proximal to the antrum in order that it should be exposed to the full effects of the acid component of the gastric juice

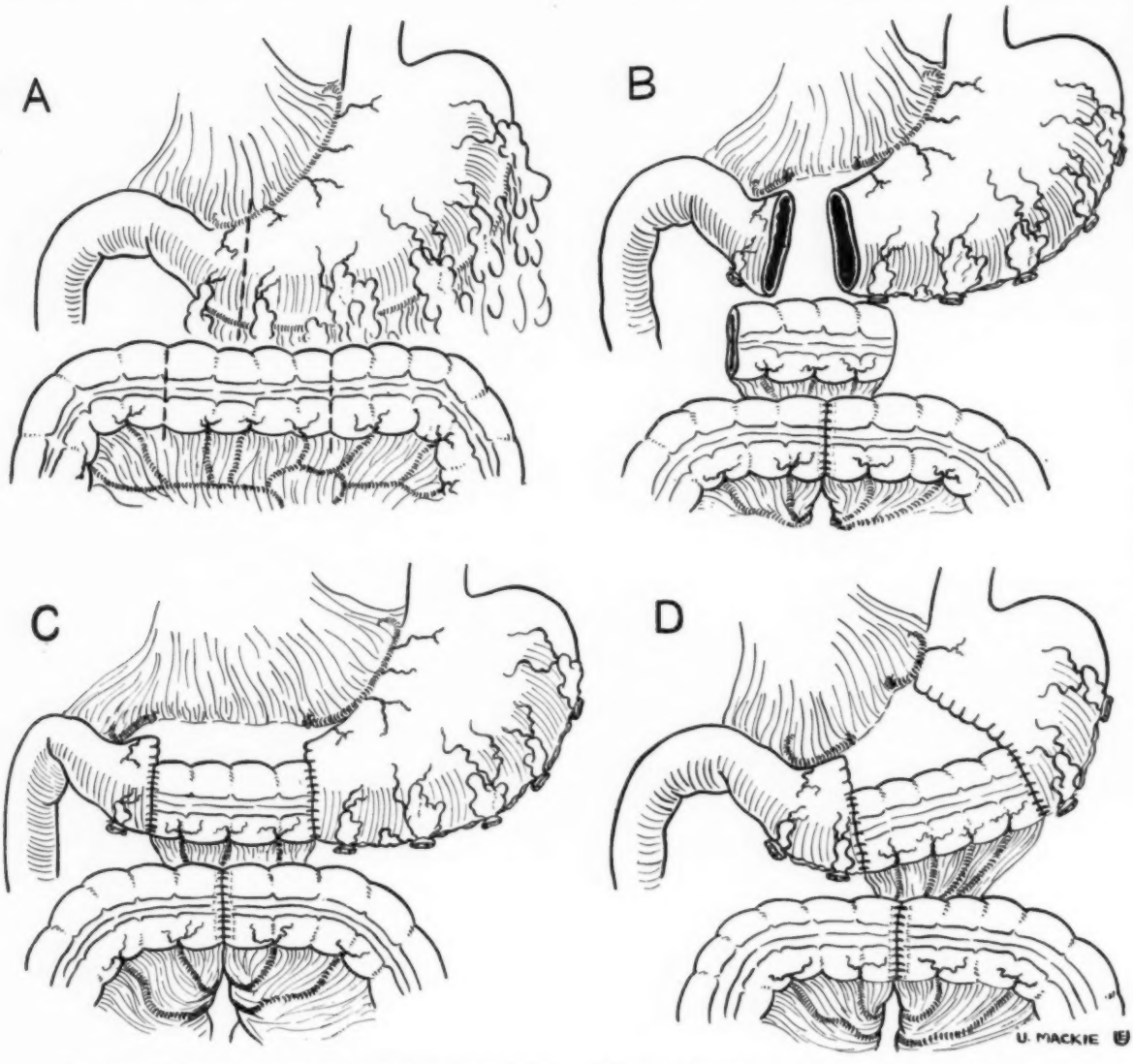


FIG. 512.—Diagram showing the technique of implantation of the colon into the stomach. A, B, Transection of stomach and colon. End-to-end colonic anastomosis. C, Final appearance in simple implantation. D, Final appearance of implantation after prior resection of part of stomach.

Group 2.—In 2 dogs a resection of the stomach was made, removing two-thirds of the acid-producing area, and the colon was then anastomosed to the fundal stump and to the antrum in anti-peristaltic fashion (*Fig.* 512 D).

Group 3.—A subtotal gastrectomy, removing seven-eighths of the acid-producing area, was carried out, together with a resection of all visible vagal nerve-fibres over the stump and up the sub-diaphragmatic portion of the œsophagus. The colon was then anastomosed antiperistaltically to the antrum and to the cardiac stump.

without the relative protection of the alkaline secretion of the antrum.

Of the 6 dogs in the first group, 3 were given daily intramuscular injections of histamine-in-beeswax, commencing two or three months after the operation. These injections cause a continuous secretion from the stomach of highly acid juice (*Group* 1a). The other 3 dogs were not given the injections (*Group* 1b).

All dogs were given antibiotics after the operation, and by the third day were back to a normal diet of meat, fish, milk, and biscuits.

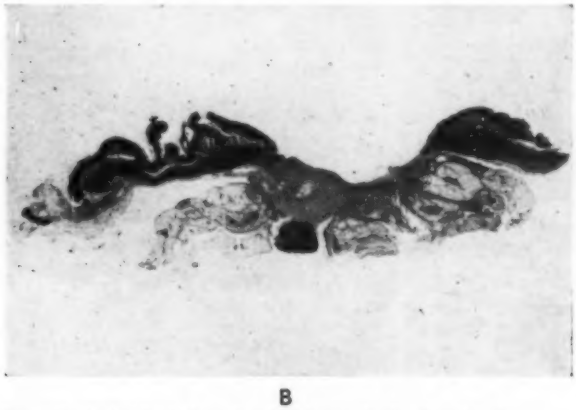
Every third day the animals were weighed, and consistent loss of weight or sustained lack of appetite were taken as the indications for laparotomy. Two dogs, however, collapsed without premonitory signs and in each case autopsy revealed a perforation of an ulcer in the implant.

It is noteworthy that in the 3 dogs in which the colonic loop had been placed in antiperistaltic fashion, regurgitation occurred immediately after each day's main meal was bolted. However, the animals would then lap up the vomitus, and all remained fit and without loss of weight until the time at which laparotomy was undertaken. Fluids were not regurgitated.

Subsequent to operation, one bitch in the first group was found to be pregnant, gestation having presumably begun just prior to the time of operation. This animal delivered itself of several live pups, and remained fit for six months after the operation, when it was sacrificed at laparotomy.

RESULTS

Group 1a. Simple Implantation of Colon into Stomach.—Two of the three dogs in this group developed large single chronic ulcers in the implant; in one the ulcer perforated only 48 hours after loss of weight was first recorded. In the third animal, the pregnant bitch mentioned above, at laparotomy six months after operation, the implant was found to be completely normal, with no trace of digestion (*Fig.* 513).



A B

FIG. 514.—A, Stomach removed at laparotomy nine weeks after colonic implantation showing large single chronic ulcer in implant (× ½). B, Section across ulcer shown macroscopically in A. Note that the histological features of the lesion are indistinguishable from those of chronic peptic ulcer in humans.

The dog in which the ulcer perforated after eleven weeks had been submitted to laparotomy six weeks beforehand; at that time the implant did not show any evidence of ulceration, but the autopsy revealed almost complete replacement of the implant by a large ulcer crater, which at one point had penetrated all coats. Vigorous pulsation was observed in the arteries in the pedicle at laparotomy on the first dog, but evidence of healing was not seen microscopically in the chronic ulcer which had penetrated the muscle layer, and considerable fibrosis was present in the extramuscular fatty tissue (*Fig.* 514).

Group 1b.—The three dogs in this group were all apparently healthy when daily intramuscular injections of histamine-in-beeswax were begun in doses increasing from 1 mg. to 2 mg. histamine base/kg. body-weight. Loss of appetite and weight were observed in each case within five days, and no further histamine was given to two of the animals. Three further daily injections had been administered to the other animal when a brisk melæna occurred and death ensued. At autopsy an extensive chronic ulcer, together with one small acute ulcer, was found in the implant. The chronic ulcer had penetrated all coats at one point on the posterior wall of the implant and dense fibrous tissue replaced the muscle coat elsewhere.

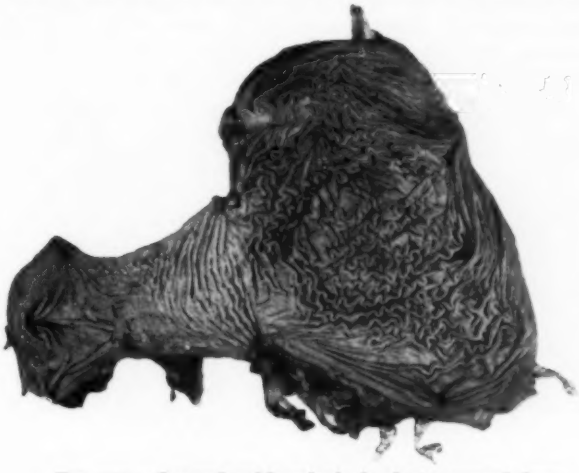


FIG. 513.—Stomach with colonic implant removed from bitch six months after operation illustrating apparent protection by pregnancy. (× ¼.)

Laparotomy was performed on the other two dogs 4 and 14 days respectively after the histamine was discontinued. In both cases vigorous pulsation of the arteries was observed in the pedicle of the implant, but the implant itself was indurated and shrunken, and most of the colonic tissue was ulcerated. In one dog the ulcer had penetrated the muscle coat, but the vessels in the base were patent (*Fig.* 515). In the other dog the muscle of the implant had been destroyed almost completely and

replaced by fibrous tissue, and the vessels in the base had undergone considerable thickening though a reduced lumen was present (*Fig.* 516).

Group 2.—The first dog of this group was explored eight weeks after the initial operation because of anorexia and weight-loss. The vessels of the colon pedicle were pulsating freely, and outwardly the implant appeared normal, but two discrete chronic ulcers were found with evidence of re-epithelialization at their edges (*Fig.* 517).

adjacent to the proximal suture line, which microscopically showed an attempt at healing by re-epithelialization from the edges (*Fig.* 519).

Summary of Results.—These are given in *Table I.*

DISCUSSION

These results show that digestion occurred when the dog's colon was exposed to the action of hydrochloric acid and pepsin. The extent of the ulceration

A B

FIG. 515.—A, Stomach removed at laparotomy nine weeks after colon implantation and nine days after injections of histamine-in-beeswax were begun, showing extensive ulceration and shrinkage of implant. A part of the colon with the end-to-end anastomosis and the pedicle to the implant can be seen below the stomach. (× ¼.) B, Section across implant shown in A. The upper specimen is from the colon of the same dog at the site of the end-to-end anastomosis to illustrate the normal colonic mucosa, and the lower specimen shows the ulceration affecting almost the whole implant, penetrating the muscle layer and with underlying dense fibrosis.

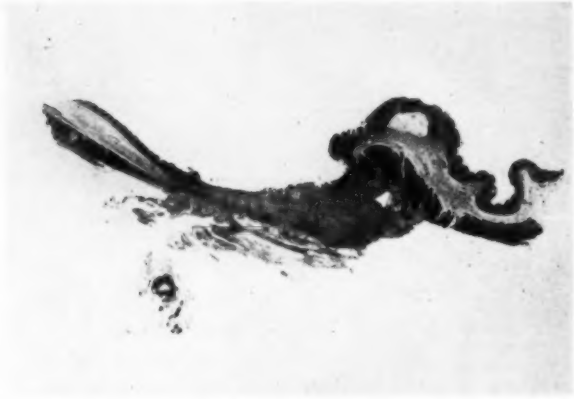


FIG. 516.—Section across chronic ulcer found in colonic implant eight weeks after operation and 14 days after a five-day course of histamine injection. The gastric mucosa is intact but the ulcer has destroyed all the layers of the colon wall and some endarteritis obliterans is present in the vessels of the ulcer base.

The second dog was well for sixteen weeks; thereafter there was loss of weight, and exploration revealed a single large chronic ulcer in the implant with re-epithelialization beginning from both colonic and gastric sides of the crater (*Fig.* 518).

Group 3.—The surviving dog of this group began to lose weight fourteen weeks after implantation, and at laparotomy the implant was found to be dilated and elongated and to have acquired a stomach-like contour, with lesser and greater curvatures. The blood-supply of the pedicle was vigorous and the mucosa of the implant was intact except for two very small ulcers immediately

bears a direct relationship to the area of the remaining parietal-cell-bearing tissue proximal to the implant, and is maximal when histamine stimulation is employed. Thus, when reduction of the proximal gastric remnant of one-eighth is combined with vagotomy, the ulceration is superficial and almost negligible in area. With histamine stimulation, the colonic implants subjected to the now continuous action of the acid juice all showed extensive ulceration of almost their entire mucosal surface. A two-thirds resection of the stomach appears to provide partial protection of the implant, and any ulceration resulting is discrete, superficial, and shows a tendency to heal.

Discrete ulcers occurred adjacent to the proximal gastrocolonic suture line, and mostly on the antimesenteric border of the transplant, at the end of the magenstrasse of the stomach (*Fig.* 514).

In none of the animals, not even those subjected to histamine bombardment, was there any evidence of ulceration of the gastric mucosa at either end of the implant, or of the duodenum although in one dog of the second group some intramucosal hæmorrhage had occurred in the wall of the stomach near the colonic ulcer. Ulcers in the implant extending to the proximal suture line stopped short of the gastric mucosa.

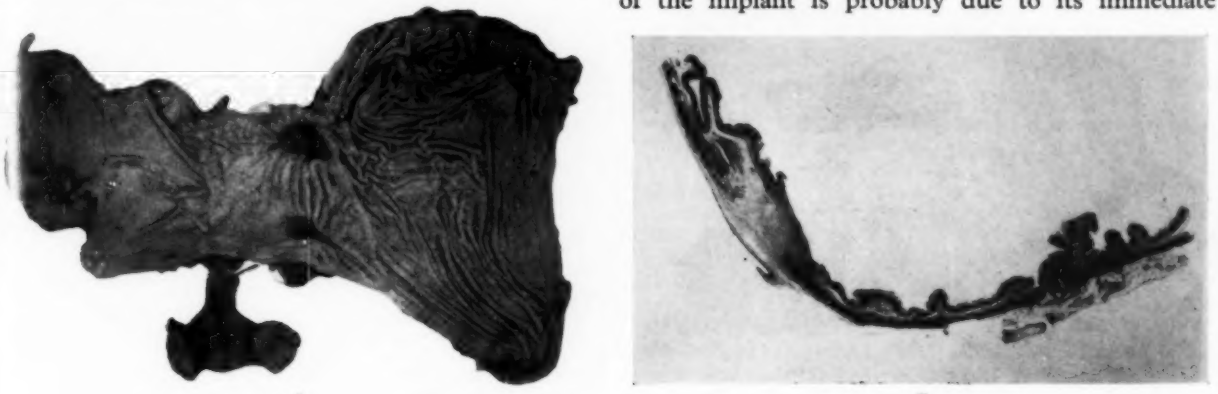
The appearance of the implant in the dog surviving the seven-eighths resection and vagotomy suggests that in consequence of the new mechanical factors the colonic loop acquires a shape similar to that of the body of the normal stomach.

The only animal in which the implant remained completely unaffected was the bitch which passed through pregnancy. Qualitative tests of the stomach contents of this dog showed the presence of acid

juice, yet the colonic mucosa was still intact four months after parturition.

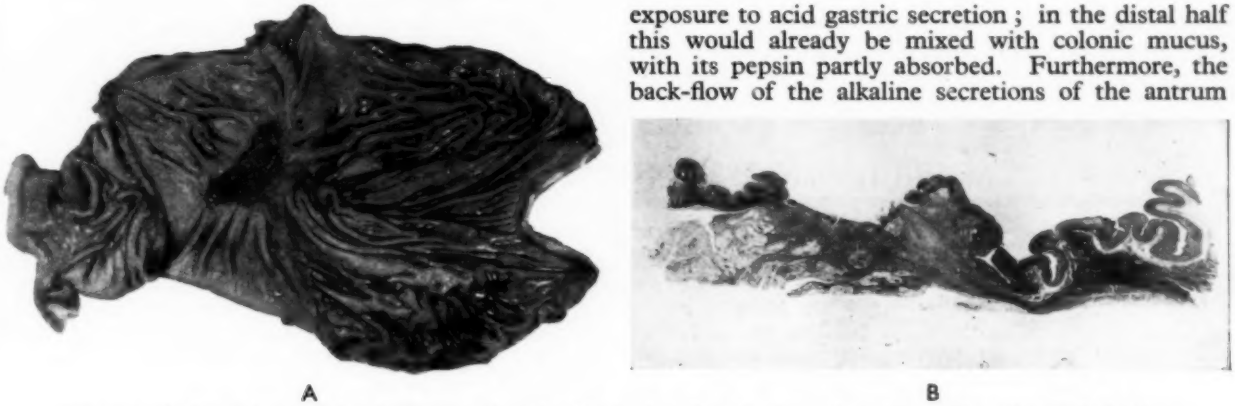
Despite a vigorous arterial supply through the pedicle, the mucosa of the implants in all cases, except that of the pregnant bitch, showed inadequate resistance to peptic digestion compared with that of immediately adjacent stomach and duodenum. The mucosa of the stomach and duodenum. Thus Davenport (1943) has reported the presence of a pepsin inhibitor in the gastric juice, and this may constitute the difference between the stomach and the rest of the alimentary tract in the resistance to peptic digestion.

The location of the ulcers in the proximal half of the implant is probably due to its immediate exposure to acid gastric secretion; in the distal half this would already be mixed with colonic mucus, with its pepsin partly absorbed. Furthermore, the back-flow of the alkaline secretions of the antrum



A B

FIG. 517.—A, Stomach removed at laparotomy eight weeks after implantation of colon and resection of two-thirds of stomach, showing two chronic ulcers in the implant. (× ⅓.) B, Section across colon implant and adjacent gastric mucosa from specimen seen in A showing discrete ulceration at orad end of the implant.



A B

FIG. 518.—A, Stomach removed at laparotomy 16 weeks after implantation of colon and partial resection of stomach showing a large single chronic ulcer in the middle of the orad half of the implant. (× ½.) B, Section across ulcer shown in A.

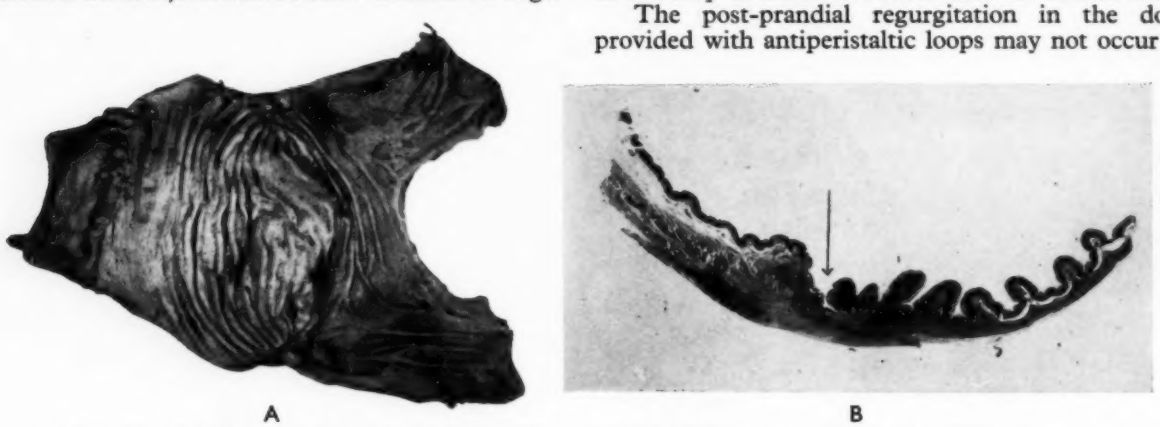
only known factors of protection against acid-pepsin digestion which the colon possesses are its ability to secrete mucus, and the capacity for epithelial cell regeneration. Mucus exposed to a *p*H below 5 suffers a reduction in viscosity and adhesiveness (Janowitz and Hollander, 1954) and whether or not the underlying epithelium is exposed to the acid-pepsin activity must then depend on the rate of its replacement. Similarly, the speed of regeneration of epithelial cells is an important factor in the process of repair. Grant (1945) has shown that when gastric erosions are experimentally produced in the cat, epithelialization occurs from the tubules at the remarkable speed of 0·2–0·4 mm. in an hour, total repair of the erosion being effected in six hours.

It may be that the rate of regeneration of mucus and of the epithelial cells in the colon is less than that in the stomach, or that the resistance to digestion of the upper alimentary tract is not a function of the physiochemical properties of mucus, nor of cell growth, but is due to some other factor intrinsic to may add to the protection. Though the ulcers were frequently at the suture line, vascular impoverishment was unlikely to be a factor, since this would be present at the distal suture line also, and in any event there was never any extension of ulceration on to the gastric mucosa adjacent to the anastomosis.

The apparent protection of the colon associated with pregnancy, despite acid secretion by the stomach, suggests that the analogous protection of the stomach and duodenum in human pregnancy may not lie in changes specific to the tissues of those organs, but to other more general factors. Ahlmark (1944) demonstrated a marked rise in blood-histaminase during pregnancy, but there is no knowledge of the histaminase content of the gastric mucosa. There is reported to be no histaminase in the gastric mucosa in the non-pregnant dog (Best and McHenry, 1930).

Pregnancy was found by Farbman, Sandweiss, and Saltzstein (1939) not to protect animals against cinchophen ulcers, and by Wangensteen (1943) not

to protect against the effects of continuous histamine stimulation; but Sandweiss and Saltzstein (1949) reported that extracts of the urine of pregnant animals provided some protection against peptic ulceration when injected into Mann-Williamson dogs.



A B

FIG. 519.—A, Specimen removed at laparotomy 14 weeks after implantation of colon, seven-eighths resection of stomach and vagotomy. The implant has become dilated and elongated and two small ulcers can be seen at the proximal gastro-colonic suture line. (× ½.) B, Section across the stomach and orad half of the implant shown in A. There is a small ulcer adjacent to the suture line overhung by the edge of colonic mucosa.

That a relationship exists between the steroid hormones and ulceration in the stomach and duodenum is suggested by the findings of reduced excretion of 11-oxysteroids during the active phase of duodenal ulceration (Sandweiss, 1951) and by the results of treatment with Kutol, an extract from the urine of pregnant mares (Paige and Heffner, 1948). Nevertheless, the output of urogastrone is unchanged during pregnancy.

The location of the ulcers on the 'lesser curve' of the implant supports the hypothesis that the appearance of most human gastric ulcers along the lesser curvature of the stomach is the consequence of mechanical trauma. This part is relatively fixed and less distensible, and possibly more exposed to mechanical stress from peristalsis and the to-and-fro movement of the gastric content.

So far as human surgery is concerned, it would seem from these results that the use of colonic loops to replace the resected part of the stomach in the treatment of peptic ulcer is only logical if simultaneously a maximum reduction of acidity is ensured by extensive resection of the parietal-cell-bearing area, together with vagotomy. When this is done, or where a total gastrectomy is performed, the colon can adequately provide a means of restoring alimentary continuity, and the result in the animal with seven-eighths resection demonstrates that alteration of the loop to a sizeable food reservoir can occur.

The post-prandial regurgitation in the dogs provided with antiperistaltic loops may not occur in human subjects; the dog habitually bolts its food, but has no difficulty in retaining the vomitus, which, by contrast, it laps up slowly and carefully.

Table I.—SUMMARY OF RESULTS

GROUP	DOG	PROCEDURE	POST-OPERATIVE SURVIVAL	EXPLORATION FINDINGS
1a	'Gypsy'	Colon implant	9 wk. to laparotomy	Single chronic ulcer in implant
	'Nero'	Colon implant	11 wk. to autopsy	Single chronic ulcer in implant
	'Snowball'	Colon implant	24 wk. to laparotomy	Implant intact
1b	'Tess'	Colon implant and histamine	12 wk. to autopsy	Two chronic ulcers in implant
	'Sandy'	Colon implant and histamine	9 wk. to laparotomy	General ulceration of implant
	'Floss'	Colon implant and histamine	8 wk. to laparotomy	General ulceration of implant
2	'Clue'	⅞ gastric resection and colon replacement	8 wk. to laparotomy	Two discrete chronic ulcers in implant
	'Monarch'	⅞ gastric resection and colon replacement	16 wk. to laparotomy	Single chronic ulcer in implant
3	'Snow-White'	⅞ gastric resection. Colon replacement. Vagotomy	14 wk. to laparotomy	Two small superficial ulcers in implant

SUMMARY

1. The resistance of the dog's colon to peptic digestion has been measured by direct anastomosis of a free loop of colon to the antral and body ends of the transected stomach. Three of the six dogs thus prepared were also subjected to injections of histamine-in-beeswax.

2. The same procedure was used in other dogs to restore continuity to the stomach after resection of two-thirds or seven-eighths of the body and fundus.

3. Ulceration occurred in the colonic implant of all the animals except one, which was pregnant.

4. The extent of ulceration bore direct relation to the area and activity of the parietal-cell-bearing part of the stomach proximal to the implant.

5. Where ulceration was minimal, evidence of adaptation of the colon implant to food reservoir function was observed.

6. It is concluded that for the purpose of colonic replacement of the stomach in human

surgery, extensive resection of the parietal-cell area, with vagotomy, would always be advisable.

I wish to thank Professor D. H. Smyth for the facilities provided in the Department of Physiology at the University of Sheffield where this work was carried out; and Dr. L. C. Hermitte, Dr. J. V. Garrett, and Dr. J. D. Hopewell, of the Department of Pathology, the Royal Infirmary, Sheffield, for their kindness in providing facilities for the preparation of the histological specimens, and for advising on them.

I am very grateful to Mr. J. Bruce and to Dr. W. I. Card for their critical appraisal of this paper.

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SHORT NOTES OF RARE OR OBSCURE CASES

PAPILLOMATA OF THE GALL-BLADDER

BY EVAN GRIFFITHS, BRIDGEND

PAPILLOMATA of the gall-bladder are rare. A review of the literature shows that most of the published cases of papillomata of the gall-bladder are unacceptable as such. Adams and Stranaham (1947) in their series of 1036 cholecystectomies describe 1 case of a benign tumour of the gall-bladder. Kerr and Lendrum (1936) in their critical analysis of the literature up to that time found they could accept only 7 cases which in their opinion represented examples of true papillomata of the gall-bladder, and severely criticized the use of the term 'papillomata' for lesions which were not neoplastic in the true sense of the word.

As shown by Shepard, Walters, and Dockerty (1942), the nomenclature of the fibro-epithelial tumours of the gall-bladder has been confused by the use of multiplicity of terms to describe the same type of tumours, and by the same term to describe different types of tumour. They referred to the growths as 'polypæ' in an attempt to distinguish them from the other polypoid lesions which had previously been described as papillomata.

This report describes a case of papillomatosis of the gall-bladder presenting with severe upper abdominal pain and jaundice.

CASE REPORT

A female, aged 67, was first seen at the Bridgend General Hospital in October, 1952. She presented as an emergency.

She gave a history of severe abdominal pain of five hours' duration, starting in the upper abdomen and in the back, the pain passing up between the shoulders. She had vomited on several occasions after the onset of the pain. She gave a history of similar attacks of pain four years prior to this admission, diagnosed as acute cholecystitis, and a similar attack again two months before admission lasting for two hours. In between the attacks she had been quite well apart from occasional flatulence.

ON EXAMINATION.—The patient appeared cyanosed, breathing between 30 to 40 to the minute; a pulse of 110, of poor volume; and a dry tongue.

There was marked guarding of the abdominal muscles —maximum in the upper abdomen. No abnormal mass could be felt. On auscultation a few bowel sounds were heard. No abnormality could be found in the cardiovascular or respiratory system. A presumptive diagnosis of acute pancreatitis was made, and the patient treated conservatively by means of continuous gastric aspiration using Ryle's tube, and a slow intravenous drip of glucose-saline. She was given pethidine for relief of pain, and continuous oxygen. The patient improved considerably with this treatment, and the suction and drip were discontinued in thirty-six hours. She had by now become clinically jaundiced. This jaundice disappeared within forty-eight hours, followed by a rapid improvement in the general condition.

A plain radiograph of the abdomen showed no evidence of gall-stones, and she was discharged for investigation as an out-patient three weeks after admission to hospital.

A diastase index two days after admission gave a normal reading.

The glucose-tolerance test was within normal limits.

On Jan. 18, 1953, she was re-admitted with a similar attack of acute abdominal pain of five hours' duration, as before in the epigastrium and in the back, and going up between the shoulders. She had again vomited on several occasions. She had been very well since her discharge. A cholecystogram performed during the interval between hospitalization had shown no filling of the gall-bladder. The clinical picture was exactly as in the previous admission; she did not, however, become jaundiced on this occasion, and the symptoms subsided completely within thirty-six hours.

A repeat cholecystogram performed on Feb. 3, again showed no filling of the gall-bladder. Liver function tests were within normal limits, with a serum-bilirubin of 0·4 mg. per cent.

In view of the previous history of cholecystitis and jaundice superimposed on a picture simulating acute pancreatitis, a laparotomy was performed on Feb. 16. A diagnosis of gall-stones having been made, possibly as an aetiological factor in an attack of acute pancreatitis.

AT OPERATION.—On Feb. 16, through a right upper paramedian incision, the gall-bladder was found to be a little larger than normal, the wall opaque and thickened, and on palpation was found to contain multiple small palpable masses, having a boggy feeling. The common bile-duct was distended, and opaque, and on aspiration was found to contain blood-stained bile. It was opened between two catgut sutures and found to be filled with numerous small pieces of papillomatous material. This material was removed, and the common bile-duct inspected on its inner aspect. No evidence was found of this papillomatous material having its origin in the wall of the common bile-duct, and was therefore assumed to have originated from within the gall-bladder and forced through the cystic duct. The pancreas felt normal and sounds were passed into the duodenum. A cholecystectomy was then done. A T tube was put into the common bile-duct, after demonstrating the patency of the ampulla of Vater and irrigating the common bile-duct. The abdomen was closed in layers, and the corrugated drain put down to the gall-bladder bed.

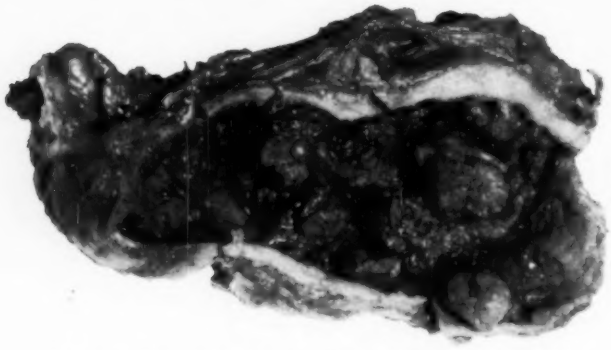

FIG. 520.—Photograph of the specimen of gall-bladder showing multiple papillomata.

The post-operative course was uneventful, the patient being discharged from hospital on the eighteenth day following operation. She has remained perfectly well since discharge.

PATHOLOGICAL REPORT.—The size of the gall-bladder removed was within normal limits, with slight thickening of its walls. It contained multiple growths, the majority in the region of the fundus, but also extending downwards into the body of the gall-bladder (*Fig.* 520). Some of these measured 1 cm. in diameter, the surface having a nodular mulberry appearance and could be seen to consist of both blunt and fine processes. Each of these larger growths was united to the wall by a narrow pedicle. There was no evidence of malignant infiltration in any of them. In between the larger papillomata the surface of the gall-bladder had small outgrowths attached to the wall by a broader base having an irregular surface consisting of fine processes. These were to be seen in the region of Hartmann's pouch, and one such growth protruded into the cystic duct. The cystic duct was found to be filled with papillomatous material. The mucous membrane of the gall-bladder in between these outgrowths appeared normal. No gall-stones were present (*Fig.* 520).

FIG. 521.—Photomicrograph of whole papilloma showing attachment to gall-bladder wall. (× 4·8.)

Histological Report.—I am indepted to Dr. D. B. Richards for the following report on the histological appearances: "The papillomata were attached to the gall-bladder wall by a thin fibrous cord and presented the features of a complex villous papilloma (*Fig.* 521). The stroma consisted mainly of thin-walled blood-vessels and in some parts of thin fibrous tissue, in parts showing hyalinization. The stroma showed infiltration by lymphocytes and plasma cells.

The epithelial components which formed the bulk of the papilloma consisted of small acini varying slightly in size, and lined by a single layer of columnar epithelium, with basal oval-shaped nuclei. This epithelium is identical with the surface epithelium of the papilloma and the lining epithelium of the gall-bladder (*Fig.* 522).

No mitotic figures were seen in the epithelium, and there was no invasion of the base of the tumour to suggest any malignancy (*Fig.* 523).

The gall-bladder wall showed thickening by fibroblastic proliferations and there was very slight infiltration by lymphocytes.

The appearances are those of complex villous papillomata of the gall-bladder."

DISCUSSION

As reported by Henry (1933) the occurrence of primary intrabiliary benign papillomata and their recognition clinically in the case of partial or complete

obstructive jaundice offers considerable difficulty in diagnosis.

Most observers agree that benign tumours of the gall-bladder do not present any characteristic clinical picture, and are not suspected pre-operatively except very occasionally as a result of cholecystographic findings. The clinical syndrome in the majority of cases is that of concomitant cholecystitis or cholelithiasis. It is most unusual for papillomata of the gall-bladder to give rise to symptoms *per se*, the presence of cholecystitis or gall-stones presenting a more logical explanation of the symptoms. In this reported case, however, no stones were present. The symptoms are accounted for by the presence of papillomata in the gall-bladder and by fragments of papillomatous material being exuded through the cystic into the common bile-duct, giving rise to severe biliary colic, with one recorded episode of jaundice due to obstruction of the common bile-duct. One similar case of gall-bladder colic produced by a papilloma obstructing the cystic duct has been described by Lund and Burman (1951).

Because of the severity of the symptoms in this reported case the condition was tentatively diagnosed as acute pancreatitis associated with intermittent jaundice.

The inability to demonstrate a functioning gall-bladder on repeated cholecystographic investigation was considered to be an aetiological factor in the attacks of pain and jaundice necessitating a laparotomy.

Kirklin (1931) was the first to stress the fact that study of cholecystographic findings occasionally enables the pre-operative diagnosis to be made. The cholecystogram shows single or multiple discrete filling defects constant in position with the patient in varying positions. These filling defects are marginal in position as shown on tangential view, and are best seen in the 24-hours film. In some cases, they are only seen in these films.

A study of the literature shows that until recently there appears to have been some considerable confusion concerning the incidence of papillomata of the gall-bladder. This appears to have been due to a confusion as to what constitutes a true papilloma of the gall-bladder.

Mayo (1915) accepted a papilloma as an associated pathological condition found in cholecystitis possibly originating as surface cracks through over-distension caused by mucous obstruction and swelling of the mucosa, incidental to cholecystitis, and associated with an inflammatory epithelial proliferation and hyperplasia. Such a condition is described by King and MacCallum (1931) as 'cholecystitis glandularis proliferans', and they stress the fact that many previously reported cases of polypæ, and papillomata are actually examples of this. Also, as pointed out by Kerr and Lendrum (1936), and Phillips (1933), Mayo described the familiar cholesterol polyp as papillomatous cholecystitis. They emphasized that a clear differentiation should be made between the familiar cholesterol polyp and the true papilloma. Kerr and Lendrum (1936) also state that the small pedunculated growths sometimes described as papillomata but histologically devoid of villus formation, and containing a high proportion of connective tissue, are probably to be looked upon as adenomatous.

FIG. 522.—Photomicrograph showing epithelial components and stroma. (× 60.)

FIG. 523.—High-power photomicrograph showing microscopical appearances. (× 120.)

The true papilloma of the gall-bladder consists of vascular connective tissue stalk covered by a single layer of tall columnar epithelium, repeated branching and re-branching of the stalk resulting in multiple villus processes, the ends of which are covered by a single layer of columnar or cubicle epithelium. The tumours may be single or multiple, sessile or pedunculated, and can measure up to 1 cm. or more in diameter.

Of the 7 fully acceptable cases in Kerr and Lendrum's series, 3 cases showed multiple papillomata. Shepard, Walters, and Dockerty (1942) classified two of their cases as papillomatosis, so extensively was the gall-bladder involved, and reported the presence of chronic inflammation and gall-stones in the majority of their cases. They suggested that these two conditions play an important role in the aetiology of the lesion. Kane, Brown, and Hoerr (1952) describe multiple papillomata in 3 cases out of 8 reported, and also stress the close association with chronic inflammation.

Brown and Cappell (1937) considered the condition to be due to the transplantation of tumour fragments as is commonly believed to occur in the urinary passages. Willis (1948), however, prefers to consider the lesions as multicentric in origin, comparable to those of the intestine and stomach.

There does not appear to be a definite known relationship between papilloma of the gall-bladder and carcinoma. Indeed, Shepard, Walters, and Dockerty (1942) say that in their opinion papilloma of the gall-bladder, unlike papilloma of the gastro-intestinal tract, rarely becomes malignant. They state that no case of malignant change in a papilloma had been reported in the literature with convincing proof. However, Kerr and Lendrum (1936), in their detailed analysis accepted two cases from the literature of papillomatous growths of the gall-bladder which they considered were definitely malignant, and that could have originated from previous benign lesions. Kirklin (1931) also confirmed the comparative rarity of this malignant change.

Tabah and McNeer (1953), however, believe that papilloma of the gall-bladder is a precancerous condition with a real danger of malignant transformation, and describe examples of true papilloma of the gall-bladder having histological evidence of malignant change occurring within the papilloma in 3 cases. They do not, however, describe evidence of invasion of the gall-bladder wall. Accumulated clinical data may well support them. It is therefore safer from a clinical point of view to regard papillomata as pre-malignant lesions.

The treatment of papilloma of the gall-bladder is cholecystectomy, because of the other pathological lesions frequently associated with this condition, and also because of the possibility of malignant change in the lesions. In this reported case the condition was also the cause *per se* of common bile-duct obstruction and intermittent jaundice.

CONCLUSION

A case of papillomatosis of the gall-bladder is described with symptoms clinically related to the papillomata.

The confusion often found in pathological diagnosis is stressed, and the rarity of the lesion emphasized.

The condition can be compared with papillomatosis of the alimentary canal and urinary tract, and is probably multicentric in origin.

The difficulty in pre-operative diagnosis is stressed, and treatment described.

I am indebted to the Pathology Department of the Welsh School of Medicine for some of the photomicrographs.

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A GANGLION IN THE MUSCLE BELLY OF PERONEUS LONGUS

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THE pathology of ganglion has been disputed and believed by various authors to be due to a neoplasm, a herniation of synovial membrane, and a mucinous degeneration of the tendinous tissue from which it arises. The latter view is now most commonly held by pathologists, and indeed Hippocrates referred to a ganglion as consisting of " mucoid flesh ".

Clinical experience and study of the literature indicate that whilst ganglion arising from the capsule of a joint, the extensor and flexor retinacula, and tendon-sheaths are common, a ganglion of the tendon itself is rare. Carp and Stout (1928), who reported on a collection of 255 personal cases of ganglion, found that 68 per cent of the cases occurred

on the dorsum of the wrist, and that as regards the tissue of origin, in 56 per cent of cases the ganglion arose from the capsule of a joint and in 23 per cent of cases from the sheath of a tendon. In no case was a ganglion found in the tendon.

This case is reported because of its interest as a problem of pre-operative diagnosis.

CASE REPORT

The patient was a man aged 54, who complained of a swelling of the outer side of the right leg, which had been present for seven months and was increasing in size. Initially he had had no pain, but in the few weeks prior to admission he had had considerable pain when walking and pain at night severe enough to keep him awake.

ON EXAMINATION.—There was a swelling in the upper third of the right leg (*Fig.* 524) in the region of the peroneus muscles. There was some weakness of the latter and also diminished cutaneous sensation over the swelling and the anterolateral surface of the leg. X-ray examination showed no involvement of the bone.

A pre-operative diagnosis was made of a fibrosarcoma or a rhabdomyosarcoma.

AT OPERATION.—The swelling was found to be entirely in the belly of the peroneus longus which was removed (*Fig.* 525).

PATHOLOGICAL REPORT.—Dr. B. S. Cardell reported on the specimen as follows: "The specimen consists of a muscle belly and tendon 15 cm. in length containing a white cyst approximately 7 cm. in diameter, whose wall is smooth and approximately 0·3 cm. in thickness. (*Fig.* 526.) At one pole is an irregular piece of yellow material approximately 3 cm. by 2 cm. by 0·5 cm. Sections show the cyst to have a dense fibrous-tissue wall. There is no specialized lining. The yellow material noted macroscopically consists of organizing fibrin in which there are groups of cholesterol clefts. Sections stained for iron were negative.

FIG. 524.—Showing the swelling in the upper third of the lateral part of the right leg.

FIG. 525.—The muscle of peroneus longus as removed at operation. The cystic nature of the swelling was evident on transillumination.

FIG. 526.—The specimen after section, showing the large cyst with a dense fibrous wall in the centre of the muscle belly.

The *histological picture* does not indicate that this lesion is an old hæmatoma or a benign connective-tissue tumour which has undergone degeneration. In another site this lesion would be interpreted as a ganglion."

I am grateful to Sir Cecil Wakeley for his encouragement and permission to publish this case.

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CHONDROSARCOMA WITH DIRECT INVASION OF THE MYOCARDIUM

REPORT OF A CASE

By J. F. HORLEY

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It is now apparent that secondary metastatic neoplasms of the heart are not as rare as was at one time supposed. Reports of metastases secondary to most primary sites have now been described, and many are listed by Lisa, Hirschorn, and Hart (1941). However, a search of the literature has failed to reveal a case similar to the one about to be described.

FIG. 527.—Portion of the left ventricular wall which the chondrosarcoma had invaded almost to the endocardium. The aortic valve cusps are visible.

CASE REPORT

The patient was a white male, aged 59.

The history of this case covers more than twenty-six years, having been admitted first in January, 1926. He complained then of a tumour which on examination was 5 cm. in diameter and attached to the costochondral junction of the fifth left rib. It was removed surgically together with an unspecified portion of the fifth rib. Microscopically it was reported as an osteochondroma.

The tumour recurred one year later and continued to grow slowly. In 1934, eight years after the first operation, it increased more rapidly in size and reached a diameter of 10 cm. It was excised with portions of the third and fourth left ribs to which, by that time, it was attached; the pleura, but not the pericardium, was attached to the mass. Microscopically, it appeared to be a chondroma. Twenty months later, in 1936, the neoplasm recurred and increased rapidly in size. At operation, it was found to be firmly attached to the pericardium over an area 7·5 cm. in diameter; it was removed with the portion of adherent pericardium and part of the third and sixth ribs, to which it was also attached. Microscopically, there was now evidence of a chondrosarcoma. In November, 1946, the neoplasm recurred at the site of the second left rib and was again excised. No recurrence took place until May, 1949, when a nodule was discovered which, clinically, and on X-ray screening, appeared to be attached to the heart. This rapidly became larger and deep X-ray therapy was tried, with little improvement, in December, 1950, and again in October, 1952, until five days before his death, which occurred on Oct. 15. Apart from complaining of his tumour as such, he had no symptoms except for some dyspnœa in the last month of his life.

AT AUTOPSY.—Examination thirty-six hours post mortem revealed a muscular, well-nourished man.

The Heart: Weight, 1247 g. (44 oz.). It was attached directly to the skin and subcutaneous tissues of the thorax by dense fibrous tissue, the anterior parts of the second to sixth ribs inclusive having been removed surgically. A mass of chondrosarcoma was growing in the wall of the left ventricle and had penetrated almost to the endocardium (*Fig.* 527). The effect was completely to immobilize the anterior and left lateral walls of the heart. The heart valves were not involved and were otherwise normal.

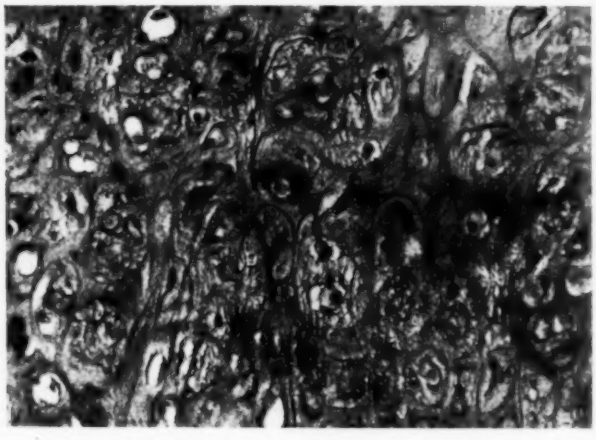

FIG. 528.—High-power view of the growing edge of the tumour. Hæmatoxylin and eosin. (× 175.)

The Lungs: Very marked pulmonary œdema was present, fluid cascading from the cut surface.

A complete examination was made of all the other organs of the body, but revealed nothing of note. In particular, no blood-borne metastasis was found.

Microscopy.—The tumour consisted of cartilaginous tissue in which scanty intercellular substance had been produced. The cells, especially at the growing edge, showed marked pleomorphism, with plentiful giant and binucleated cells (*Fig.* 528). The tumour was advancing by causing compression and necrosis of the myocardium in contact with it and no infiltration between individual muscle-fibres was seen (*Fig.* 529). The appearances were those of a chondrosarcoma invading the myocardium.

DISCUSSION

This case appears to be unique. Schmorl (1907), Fry and Shattock (1926), Kosa (1929), and De Loach and Haynes (1953) each have described remarkable

ases in which chondrosarcomata have grown by irect extension from their primary sites via the egional veins into the inferior vena cava, along whose umen they have extended into the right atrium, right

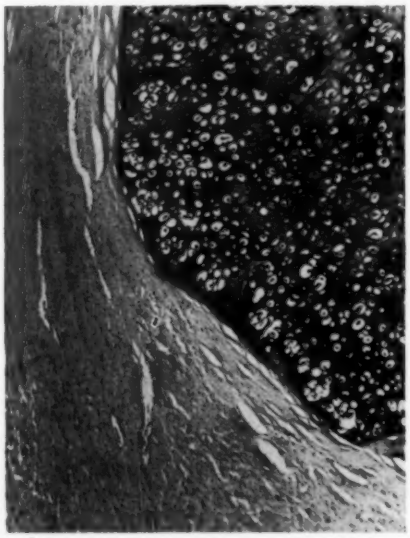

FIG. 529.—Low-power view of the junction line between the tumour and myocardium. Hæmatoxylin and eosin. (× 33·3.)

ventricle, and even into the main pulmonary artery. However, in these cases the tumour has been contained by the endocardium and, although within the chambers of the heart, no invasion of the myocardium has occurred. The only other occasion in which a record of myocardial invasion by a chondrosarcoma has been traced, is the allusion, in a paper by Lichtenstein and Jaffe (1943), to a case dying in another hospital and not actually examined by them. In this case, a blood-borne metastasis had occurred.

Lichtenstein and Jaffe (1943), in an excellent review of chondrosarcomata, emphasize the tendency they possess for recurrence locally after apparently complete removal. These authors advise wide local excision and, in the case of chondrosarcomata of the ribs, that at least one healthy rib on each side of the affected one should be removed. They describe a patient very similar to the case reported here from whom an osteochondroma of the third costochondral junction was removed, only to recur at the same site after three years. A very extensive removal was then undertaken and Mayer (1941), followed up the case and reported that there was no recurrence after five years. The case described here, where in the first instance only narrow local removal was performed, illustrates the inexorable advance of these slow-growing tumours. Nevertheless the patient lived for twenty-six years after the first operation, so that his treatment, while not perhaps a complete success, cannot be described as a failure.

SUMMARY

A case is described in which a chondrosarcoma initially of the fifth left costochondral junction invaded the myocardium. It had advanced slowly during a period of twenty-six years in spite of repeated attempts at surgical removal. No record of a similar case has been discovered in the literature.

I wish to thank Mr. Griffiths, under whose care the patient was so often admitted, for permission to use his case notes. It is a pleasure to thank Dr. Kemball Price for his criticism and advice during the preparation of this paper. Mr. Jackson kindly supplied the photographs.

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LARGE TRICHOBEZOAR IN CHILDHOOD

REPORT OF A CASE

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ALTHOUGH bezoars have been recognized and treated since the eighteenth century, they are in these days seen but rarely. DeBakey and Ochsner (1938, 1939) reviewed 171 cases of trichobezoar and included 1 case of their own. Osmond and Price (1951) recorded 13 more cases up to December, 1948. Since then 17 more cases have been published in the literature, making the total to 202 until 1951.

Although the bezoars are reported to have been used in Hindu medicine since the twelfth century (Aird, 1949), only 1 case has been seen in this institution in thirty-eight years among about 36,000 patients treated in the Department of Surgery.

CASE REPORT

A girl, V. R., aged 7 years, was admitted to Lady Hardinge Medical College Hospital, New Delhi, on Sept. 10, 1953, with an 'abdominal tumour'. The child's mother had noticed a swelling for three years, which had been gradually increasing in size. There was no history of pain, vomiting, fever, or loss of weight, or any other complaints. Her appetite was very good and her bowels normal. Both the parents and her sister were healthy. Her father worked as a cobbler and was very poor. She lived in a miserable hovel and depended for food on the roadside dustbins. Although on repeated questioning she denied eating hair, a few days after admission to the hospital she was found chewing her own

hair. Her mother then remarked that it was for this reason that she had cut her child's hair short.

ON EXAMINATION.—The patient was a well-developed healthy child. There was no sign of malnutrition (*Fig.* 530). She was rather shy at first, but was otherwise mentally normal. There was distension of the abdomen, which was more marked in the upper half. A smooth

FIG. 530.—A photograph of the patient showing the outline of the abdominal mass.

firm mass was palpable, extending from the left to the right hypochondrium. It felt rather doughy and was not tender. Its lower convex border reached to the level of the umbilicus. Along its upper border a sharp notch was palpable to the right of the midline, simulating a splenic notch. A diagnosis of splenomegaly had been made before admission. The tumour was mobile from side to side, but did not move with respiration. During the period of observation no alteration in shape, size, or position of the tumour was detected. All the other systems were normal.

Blood examination: Hb 12·1 g., R.B.C. 4,000,000 per c.mm. (polymorphonuclears 50 per cent, lymphocytes 26 per cent, eosinophils 24 per cent.)

Stool examination: No hair seen; ankylostoma ova present.

Radiological Findings.—The outline of the distended stomach was visualized by the barium, which was seen to trickle along the lesser curvature and to diffuse through the mass, outlining the tumour wall, which filled almost the entire lumen of the stomach. There was no stomach air bubble (*Fig.* 531).

In contrast with this, the radiograph taken a month later, after the operation, showed the stomach normal in shape, size, and motility, with gas in the fundus (*Fig.* 532). A pre-operative diagnosis of hairball was made. The operation was delayed on account of ankylostoma infection, which was treated with two courses of tetrachlorethylene.

AT OPERATION (Oct. 26).—Through a left paramedian incision a markedly distended stomach was exposed; it occupied almost the entire abdominal cavity. A horizontal incision 10 cm. long was made on the anterior surface of the stomach along its long axis. A greenish black mass with a slimy shining surface was found to fill the entire lumen; there was hardly any space between it and the wall of the stomach. With some difficulty the mass was delivered, first from the cardiac end of the stomach, and then from the duodenum. The mucosa and the muscle layers were greatly hypertrophied. No ulcers were seen on the mucous surface, although it

FIG. 531.—Barium meal before operation showing markedly distended stomach and absence of gas.

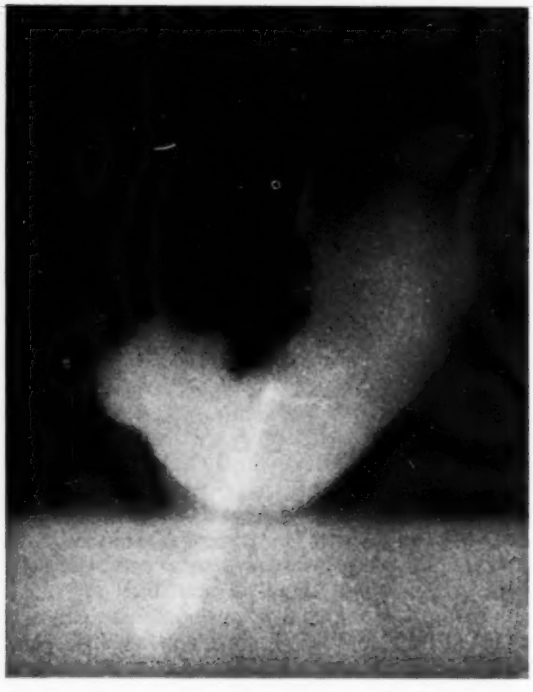

FIG. 532.—Barium meal one month after operation showing normal appearance of the stomach with gas in the region of fundus

appeared congested. The stomach was sutured in two layers and the abdomen was closed.

The specimen formed a complete cast of the stomach and proximal two-thirds of the duodenum with a C-shaped curve at its distal end which was bile-stained. While wet it weighed 2·1 kg., and measured 23 cm. in length and 17 cm. in width (*Fig.* 533). It consisted of a mesh of

FIG. 533.—Operation specimen of trichobezoar with C-shaped curve at its distal end.

matted human hair with particles of food adherent to it and covered with mucoid-like material.

Post-operative recovery was uneventful, and she was discharged three weeks later. The patient was seen again in March, 1954, four months after the operation. Her general condition was very good, and she had gained 2 kg. in weight. However, as trichophagia persisted, she was re-admitted for barium meal examination and gastric analysis to exclude recurrence. Both the investigations were normal.

DISCUSSION

Aetiologically this case is interesting. An enormous trichobezoar in a child without any symptoms is very rare. Sawyer, Coppinger, and Nelson (1950) reported a case of trichobezoar in a girl aged 4½ years, but she suffered from vomiting. Fox and Stiles's (1951) patient aged 4 years had symptoms of pain in the abdomen and anorexia.

The process of formation of a 'hair ball' probably takes years before it becomes palpable and gives rise to symptoms, which probably accounts for its infrequency in young children. The majority of cases are found in females between 10 and 30 years of age. It is, therefore, possible to overlook this condition in childhood. According to Hurwitz and McAlenney (1951), this condition should be considered in differential diagnosis of gastro-intestinal disorders in childhood.

The actual cause of trichophagia is not known, but in this case the patient's social and environmental conditions were important factors in its development. It may have been done to appease hunger or may have developed as a bad habit, like nail-biting. It is said that animals with perverted appetite have been cured when the missing dietary elements have been supplied. This may not be applicable to humans, but trichophagia was checked in this case as long as she stayed in hospital and had plenty of nourishing food. On returning to her home she reverted to the habit of chewing hair. Hairballs may recur several times after an interval of years; various authors have recorded such cases.

Diagnostically this case is of interest because of resemblance of the abdominal tumour to an enlarged spleen. The latter is commonly seen in this country.

Nussey and Leask (1949) found crepitus on palpation, and consider this an important sign in the diagnosis of trichobezoar, but it was absent in this case. The presence of a smooth firm mass in the hypochondrium extending to the epigastrium is the most important and constant finding in the great majority of cases. DeBakey and Ochsner (1938) noted a palpable tumour in the abdomen in 87·7 per cent of the patients. A clear history of trichophagia is very helpful in suggesting the diagnosis, but it is not always available. Wilkinson and Wilkinson (1950) found it in 50 per cent of the patients.

Certain investigations are useful in diagnosis, such as radiography, particularly in doubtful cases. The mass can be visualized but unlike other intragastric masses it does not produce a filling defect since some of the meal trickles through the hair mesh giving a mottled appearance (Schwartzman, 1937).

There is usually achlorhydria on gastric analysis, as in this patient, and it is the common experience that the gastric acidity returns to normal after removal of the trichobezoar. Hair is not always detected in the gastric contents.

The blood-picture is helpful in excluding splenomegaly associated with blood changes. Slight secondary anæmia and eosinophilia in this case were due to ankylostomiasis, and responded to treatment. According to DeBakey and Ochsner (1939), only 3 cases have been reported with helminthiasis.

Although the trichobezoar in this case had filled not only the lumen of the stomach but also the greater part of the duodenum, yet the patient had no symptoms of gastric or duodenal obstruction in spite of almost complete blockage. In such cases removal should be complete and in one piece, as there is danger of a piece being left behind and causing further complications, such as recurrences and obstruction.

SUMMARY

A case of symptomless large trichobezoar in a girl of 7 years is described. The tumour was diagnosed as splenomegaly by different doctors. Pre-operative diagnosis of trichobezoar was made, and it was successfully removed by operation. Recovery was uneventful.

A brief review of historical and diagnostic interest is made.

I wish to express my thanks to Mr. M. R. Ewing, of the Postgraduate Medical School of London, for his valuable advice.

ADDENDUM

The girl V. R., now aged 9 years, was re-admitted to the hospital on Sept. 1, 1955, owing to the re-appearance of the swelling in the upper abdomen which has

gradually increased in size for one year, and for occasional pain in the epigastrium unrelated to meals for two months. She confessed this time that she had continued to eat hair after she was discharged from the hospital about eighteen months ago. The patient was last seen at the follow-up clinic in February, 1954, when both the gastric analysis and barium meal examinations were normal.

FIG. 534.—The second trichobezoar, removed in September, 1955.

On admission this time she was wasted and anæmic, her hæmoglobin was only 6·5 g., otherwise she was quite alert and bright. On examination a large firm mass very similar to the previous one removed in 1953, was palpable across the upper abdomen, extending from the left to the right hypochondrium; its lower margin was at the level of the umbilicus. The mass was dull on percussion, but on the whole it was less prominent than the previous one.

Straight X-ray examination of the abdomen showed a diffuse opaque shadow in the region of the stomach. On barium meal examination the stomach was outlined, but the body seemed to be filled with an intragastric mass. In view of the findings at the previous operation in November, 1953, and history of trichophagia the diagnosis of trichobezoar was easily made.

The patient was treated for anæmia with iron intravenously and was given 400 c.c. of blood; her hæmoglobin improved to 11 g. But while in the hospital she once had severe abdominal pain followed by a large vomit containing only food matter but no hair. On examination there was a localized area of tenderness over the epigastrium in the midline just above the upper border of the mass.

Operation was performed on Sept. 12, when the abdomen was opened through the previous scar; some adhesions were found between the anterior surface of the stomach and the parietal peritoneum, and these were separated; the previous scar in the stomach was invisible. The organ was opened by a horizontal incision about 10 cm. in length along it long axis. A greenish black mass was found filling the entire lumen of the stomach; it was delivered from the fundus, body, and pyloric end by hand, its long tapering end, 34 cm. in length, extending in to the intestine. The specimen (*Fig.* 534) formed a complete cast of the stomach similar to the one removed in 1953, but it was narrower, although much longer, than the previous specimen, its total length being 67·5 cm., and its maximum vertical measurement 20·5 cm. It weighed 1 kg. while wet.

On removal of the mass a small circular ulcer 1·5 cm. in diameter, with inflamed margins, was seen on the posterior surface of the body of the stomach close to the lesser curvature. As it was considered to be due to mechanical trauma and the gastric lumen was septic no further surgery was done for the ulcer, and the gastrotomy wound was closed in three layers. During the operation the patient was given 500 c.c. of blood, and post-operatively gastric suction was continued for 36 hours; milk feeds were then started. She had an uneventful recovery.

Barium meal examination a month later showed no sign of the ulcer crater. The child has gained 4 kg. in weight since the operation two months ago. This case is of particular interest that within a short period of less than two years another large trichobezoar should have been formed in a young child. Besides the risk of complications on account of the ulcer, such as perforation or hæmorrhage, there was also danger of intestinal obstruction as the terminal part of the long bezoar had extended into the jejunum. This case undoubtedly requires institutional psychotherapy to control her habit of trichophagia.

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REVIEWS AND NOTICES OF BOOKS

ar, Nose and Throat Nursing. By F. BOYES KORKIS, M.B., Ch.B., D.L.O., F.R.C.S., F.I.C.S., Surgeon, Metropolitan Ear, Nose, and Throat Hospital. 8 × 5⅛ in. Pp. 168 + viii, with 85 illustrations. 1955. London: J. & A. Churchill Ltd. 12s. 6d.

HE most useful section of this short book is that devoted the description of out-patient procedures; excellent so is the common sense advice given to nurses conducting patients from operating theatre back to ward. The tionale of common E.N.T. operations is described nortly and with commendable clarity. The general escription of E.N.T. diseases reads rather like an inentory and is dull; one or two rare conditions could ave been omitted with advantage. When dealing with perations, the author writes nothing about guillotine onsillectomy on the grounds that it is outdated. This s a pity, for in many densely populated areas this peration is routine because long lists demand speed.

The heading " mucocele of the nose " is an obvious misprint which should be corrected in the next edition. There are several startling examples of bad English such as " to obtain satisfactory visualization of the nose " on page 99. The main part of the preface was missing from the copy presented for review.

Cardiovascular Surgery. Studies in Physiology, Diagnosis, and Techniques. Being the Proceedings of the Symposium held at Henry Ford Hospital, Detroit, Michigan, March, 1955. Edited by CONRAD R. LAM, M.D., Surgeon-in-Charge, Division of Thoracic Surgery, Henry Ford Hospital. 9¾ × 6¼ in. Pp. 543 + xxix, with numerous illustrations. 1955. Philadelphia and London: W. B. Saunders Co. 89s.

THIS is quite the best symposium that has ever been published on cardiovascular surgery and Dr. Conrad Lam deserves much credit for the way in which he produced it. With some sixty participants from different parts of the world all taking part in a large symposium on a special subject, it is no easy matter to edit the various papers.

Every facet of cardiovascular surgery has been discussed in much detail and the various drawings and pictures which illustrate the different chapters are of excellent quality. Sir Russell Brock, who writes an interesting foreword to this work, stresses the international character of the book, and he also takes part in the discussion on pulmonary stenosis. Professor Rob deals in a masterly way on substitutes for arterial segments and discusses his method of freeze-drying the arterial grafts.

Although there has been a tendency to decry symposia in this country, yet, if they were of the same standard as that which took place at Henry Ford Hospital in March, 1955, there could be little with which to find fault.

Text-book of Orthopædic Medicine. By JAMES CYRIAX, M.D., M.R.C.P., Physician to the Department of Physical Medicine, St. Thomas's Hospital, London. Fifth edition. Vol. I. Treatment by Manipulation and Massage. 8½ × 5½ in. Pp. 373 + xvi, with 127 illustrations. 1955. London: Cassell & Co., Ltd. 21s.

THE fifth edition of this well-illustrated text-book portrays the various techniques of manipulation and massage that are at present in vogue at St. Thomas's Hospital. These methods are used in order to restore painless mobility to the moving parts of the body.

Surgeons as a whole will be interested in the special chapter on friction for varicose ulcers, and that on the use of massage in plastic surgery.

Body Fluids in Surgery. By A. W. WILKINSON, Ch.M., F.R.C.S.E., Senior Lecturer in Surgery, University of Aberdeen; etc. 8½ × 5½ in. Pp. 212 + x, with 6 illustrations. 1955. Edinburgh: E. & S. Livingstone Ltd. 16s.

ALTHOUGH a new understanding of fluid physiology has been made possible by isotope studies and other technical advances, this book approaches the problem of body fluids from the clinical standpoint. The importance of the 'lean tissue mass' on calculation of the total body water is stressed, and it is pointed out how the latter is based not on the actual weight but on the 'ideal body weight', which varies with sex, height, and age, and can be obtained from standard tables. The author emphasizes the modern view that the cell membrane is permeable to cations and that it is in no sense the cell membrane barrier which keeps sodium mainly in the extracellular fluids and potassium in the intracellular. When discussing water loss a distinction is made between water lost by evaporation and by sweat, a difference which is not always appreciated. As an index of the clinical bias which this book maintains, we read, for instance, that " the use of rubber sheeting should be abandoned because this creates a private environment around the patient of 100 per cent humidity at body temperature and is equivalent to putting the child in a turkish bath "; and again the taste of the sweat is mentioned as an indication of the sodium level. There are good clinical accounts of water intoxication, sodium poisoning, and water and salt depletion. Potassium metabolism is fully dealt with, and a useful clinical picture is given of potassium deficiency. The dangers of intravenous potassium are stressed. The metabolic effects of injury and surgery are described, and the views of Selye are epitomized usefully.

In discussing shock the author divides this into neurogenic shock and shock due to fluid loss. In the account of the clinical management of this condition there are warnings against the use of cradles and the prescribing of large volumes of fluid to drink, because this is likely to lead to vomiting in the shocked state. It is surprising that, in a discussion of the transfusion treatment of shock, no mention is made of intra-arterial transfusion and that this only receives the most peremptory treatment, almost as an afterthought on the last page; even then this sometimes life-saving measure is not recommended.

The crush syndrome is discussed and there is a chapter on the effects of the loss of gastro-intestinal secretions whether by vomiting, fistula, or paralytic ileus. The metabolic effects of ureteric implantation are described as being due to acidosis from the absorption of chloride by the colon, and it is recommended that this should be treated by colonic drainage. The influences of associated diseases of the heart, liver, and kidney are fully described and there is an excellent discussion on plasma substitutes. It is pointed out how if in the substitute there is too high a proportion of molecules of low molecular weight it is rapidly diffused and secreted. If, on the other hand, there is too high a proportion of molecules of high molecular weight this leads to increased viscosity and sedimentation of corpuscles. The ideal molecular weight is held to be between 40,000 and 120,000. Various substitutes are discussed and the best is probably 6 per

cent dextran in 0·9 per cent saline. Dextran is a polysaccharide which, by differential fractionation of the hydrolysed product, has recently been so confined within the limiting molecular weights that only about 10 per cent is excreted in 24 hours. It is pointed out how all these substitutes tend to upset blood grouping, and methods for ameliorating this disadvantage are suggested.

This is an excellent book for house officers and can be recommended unreservedly.

Local Analgesia: Head and Neck. By Sir ROBERT MACINTOSH, D.M., F.R.C.S. (Edin.), F.F.A.R.C.S., Nuffield Professor of Anæsthetics, University of Oxford; and MARY OSTLERE, M.B., M.R.C.P.E., F.F.A.R.C.S., Research Assistant, Nuffield Department of Anæsthetics, University of Oxford. 8⅝ × 5⅞ in. Pp. 138 + viii, with 145 illustrations by Marjorie Beck, some coloured. 1955. Edinburgh: E. & S. Livingstone Ltd. 27s. 6d.

MORE than half the pages of this excellent monograph are devoted to a detailed description of the anatomy of the head and neck, and this is admirably supplemented by a series of original illustrations which greatly aid the reader in understanding the precise anatomical details.

The technique of analgesia is dealt with in considerable detail and we should especially congratulate the authors upon the admirable description of the various techniques available for bronchoscopy.

This book is excellently produced and the illustrations are clear and useful. We recommend this book to all candidates studying for the F.F.A. and D.A. diplomas.

Subphrenic Abscess. By H. R. S. HARLEY, M.S., F.R.C.S., Consultant Thoracic Surgeon to the United Cardiff Hospitals and to the Welsh Regional Hospital Board. 8½ × 5½ in. Pp. 216 + xii, with 41 illustrations. 1955. Oxford: Blackwell Scientific Publications. 35s.

FOR a number of years Mr. Harley has made a detailed study of the problem of subphrenic abscess and the above monograph represents the result of this industry. The author deals with the problem from every point of view. The chapter on pathology is particularly interesting and the views of Overholt on the movement of fluids within the peritoneal cavity, together with the effect on these of the Fowler position as described by Spalding, are given full weight. In the chapter on the clinical aspect of this condition, the classical three zones of 'dullness-resonance-dullness' were not found in any of the 188 cases in the series. The interesting observation is made that left-sided subphrenic abscesses are not necessarily associated with fixity of the diaphragm, but on the right side this is an almost invariable accompaniment. Radiographs showed gas in the abscess in only 28 per cent of cases. This was more likely to be seen in the lateral than the anteroposterior films, and when observed was excellent evidence for localization. Mostly this gas was due to perforation of gut or lung and only very occasionally to the generation of gas by gas-forming organisms. A useful chapter on the common condition of subphrenitis is appended, and when suppuration is suspected exploratory aspiration, at least in the ward, is not recommended as a diagnostic procedure because it is both unreliable and risky. Exploratory aspiration in the operating theatre followed immediately by operation is not so definitely to be condemned, but if operation is to be undertaken in any case, localization by radiography will almost certainly have been sufficiently accurate to render this somewhat risky procedure unnecessary.

The surgical techniques for dealing with this condition are described and the extraperitoneal or pleural approaches are recommended as being by far the safest, as the mortality-rates show. It is rather disheartening that the mortality of subphrenic abscess remains at about 40 per cent despite all advances in chemotherapy. In extraperitoneal subphrenic abscess, however, the mortality is as low as 7 per cent.

A small criticism in production might be entered in that the illustrations are all gathered together at the end of the book and this is rather a nuisance when reading the text.

The bibliography is good and the whole essay may be considered a standard work on this very difficult problem.

Fractures of the Facial Skeleton. By N. L. ROWE F.D.S. R.C.S., L.R.C.P., M.R.C.S., L.M.S.S.A., H.D.D. R.C.S.; and H. C. KILLEY, F.D.S. R.C.S., L.R.C.P., M.R.C.S., L.M.S.S.A., H.D.D. R.C.S., Consultants in Oral Surgery, Plastic and Maxillo-facial Surgery Unit, Rooksdown House, Basingstoke. With a Foreword by Sir REGINALD WATSON-JONES. 9¾ × 6¾ in. Pp. 923 + xxxvi, with 1231 illustrations, 14 in colour. 1955. Edinburgh: E. & S. Livingstone Ltd. £6.

THIS work is in many ways unique, for it is the outcome of practical teamwork by two experienced dental surgeons who have been helped by specialists in plastic, orthopædic, and ophthalmic surgery. Until recently faciomaxillary surgery was in its infancy and the second world war brought it into prominence. Owing chiefly to the foresight of Sir Harold Gillies, the plastic centre at Rooksdown House, Basingstoke, came into existence after the war started and very soon became the centre for plastic surgeons both at home and abroad.

At the end of the war the need for this centre to continue its work was evident, for the many and various traumatic injuries to the face appeared to increase in what may be called a mechanical and traumatic age.

The authors of this excellent work have an extensive practical experience in fractures of the facial skeleton and they have given the best of their far-reaching knowledge. The written text is beautifully illustrated with no less than 1231 pictures, of which 14 are in full colour.

The volume is divided into three main parts: The first is devoted to the applied surgical anatomy of the mandible, fractures and their treatment. Part II deals in an admirable and practical way with fractures of the middle third of the facial skeleton, while Part III is devoted to the treatment of gunshot wounds of the face and jaws.

An excellent production of which British Surgery may well be proud.

Diseases of the Nose and Throat. A Textbook for Students and Practitioners. By Sir ST. CLAIR THOMSON, M.D., F.R.C.P., F.R.C.S. Revised by V. E. NEGUS, D.Sc., M.S., F.R.C.S., Consulting Surgeon for Diseases of the Ear, Nose, and Throat, King's College Hospital; with the assistance of G. H. BATEMAN, M.A., B.M., B.Ch., F.R.C.S., Surgeon to the Ear, Nose, and Throat Department, St. Thomas's Hospital, London. Sixth edition. 9½ × 6½ in. Pp. 1040 + xvi, with 46 Plates, some coloured, and 353 illustrations. 1955. London: Cassell & Co. Ltd. 90s.

WHEN this standard work first appeared in 1911 it was hailed as the best text-book available in the English language. As each new edition has been published the same comment has been made and the book appears to have gone from strength to strength.

In the new sixth edition the matured clinical experience of Mr. Victor Negus has more than ever come to the fore.

There is a new section on stridor in childhood which is very interesting and useful, and there has been clarification on the subjects of congenital glottic stenosis and laryngismus stridulus.

Many new operations on the larynx, especially for malignant disease, have been incorporated.

There is little room for criticism in this edition and it will long remain a great credit to British surgery. It is the standard work of reference the world over.

Living Bone in Health and Disease. By IRVIN STEIN, A.B., M.D., F.A.C.S., F.I.C.S., Assistant Professor of Orthopedic Surgery, University of Pennsylvania, etc.; RAYMOND O. STEIN, A.B., M.D., F.I.C.S., Assistant in Orthopedics, Hahnemann Medical School; and MARTIN L. BELLER, A.B., M.D., Instructor in Orthopedics, Hahnemann Medical School. 10 × 7 in. Pp. 510 + xii, with 387 illustrations. 1955. London: Pitman Medical Publishing Co., Ltd. £5 10s.

THIS is a useful reference volume on an all-important subject, the book is lavishly illustrated with photomicrographs, radiographs, and clinical and macroscopical photographs. Every known bone condition or disease is discussed at length and the various biological processes of bone have been considered in detail.

The first part of the book deals with the structure, function, and reactions of normal living bone. In this there is an able discussion on the part played by vitamins, minerals, hormones, and physical agents in relation to bone.

The second part of the work is concerned with the common derangements of the skeletal system, while the third part is devoted to a consideration of the diagnostic classification of bone diseases.

At the end of each chapter there is a series of references covering the subject considered in the chapter. It must be stated that the majority of the references refer to American literature.

The real value of this work is as a reference volume where one may find a detailed account of any bone disease.

The Surgery of Theodoric, *ca.* A.D. 1267. Translated from the Latin by ELDRIDGE CAMPBELL, M.D., and JAMES COLTON, M.A. Volume I, Books I and II. 8⅜ × 5½ in. Pp. 223 + xi, with coloured frontispiece. 1955. New York: Appleton-Century-Crofts Inc.

IT is always interesting to read about the treatment of diseases many centuries ago and the present volume deals with the practice of surgery about A.D. 1267.

It is curious that the treatment of fractures and wounds differed very little in all basic principles from those in vogue to-day, with the exception of the absence of the antibiotics. The setting of fractures and the reduction of dislocations was very practical and this was performed without the use of radiographs.

Wine and oil seem to have been the common dressings used at this period, and the surgeon is constantly told to be very gentle in the use of instruments and in the care of the wound.

The most fascinating chapter in the book is devoted to the method of extracting arrows from the various parts of the body and the instructions are very practical and differ little from those we should employ to-day.

We are apt to think that the débridement of wounds and secondary suture are the result of two modern wars, but they were practised by Theodoric in the thirteenth century.

A very interesting book.

The Year Book of General Surgery, 1955-1956. Edited by EVARTS A. GRAHAM, A.B., M.D., Emeritus Professor of Surgery, Washington University School of Medicine. With a Section on Anesthesia edited by STUART C. CULLEN, M.D., Professor of Surgery and Chairman of Division of Anesthesiology, State University of Iowa College of Medicine and Hospitals. 7½ × 5 in. Pp. 655, with 182 illustrations. 1955. Chicago: Year Book Publishers Inc. (London: Interscience Publishers Ltd.) 45s.

WE have come to recognize this year book as an interesting and practical summary of surgical progress and research compiled by an elder statesman in all surgical affairs. The many and varied abstracts of published surgical literature are of the highest quality and interest to surgeons both at home and abroad, and Evarts Graham has the happy knack of sifting the wheat from the straw, and only gives a précis of important papers from the literature.

The face of surgery is always changing and it is because of this very fact that this year book is of such value to surgeons generally. Few surgeons to-day have the time or inclination to read the international surgical literature and therefore to have all the worthwhile papers abstracted and published in book form is of real value.

An excellent book and one which will repay reading.

Medical Photography. Radiographic and Clinical. By T. A. LONGMORE, Hon.F.S.R., Principal, Kodak School of Medical Radiography and Clinical Photography; etc. With a Foreword by Brigadier D. B. MCGRIGOR, O.B.E., M.B., Ch.B., D.M.F.E., Hon. F.S.R., Consulting Radiologist, The War Office. Fifth edition. 7¼ × 4¾ in. Pp. 990, with 320 illustrations in the text and 76 as plates. 1955. London and New York: The Focal Press. 60s.

IT is a pleasure to see the new fifth edition of this important work. The whole medical profession is to-day "photography minded", and rightly so, for good photographs enhance the written word in no uncertain fashion. It is curious to consider that this book is the only comprehensive work on medical photography in any language, and was first published during the last war.

To-day most hospitals have a photographic department and each year this department becomes more important to the whole of the medical staff. Surgical research and technique are dependent in no small way on good photography.

This fifth edition has been very carefully revised and the sections on colour and flash have been re-written, and there is also information on the latest cameras.

An indispensable reference book on medical photography.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Analgesia for Midwives. By HILDA ROBERTS, M.R.C.S., F.F.A. R.C.S., D.A., D.C.H., Hon. Research Assistant, Institute of Obstetrics and Gynæcology, Hammersmith Hospital, London. 8½ × 5½ in. Pp. 68 + viii, with 25 illustrations and 5 coloured plates. 1955. Edinburgh: E. & S. Livingstone Ltd. 10s. 6d.

The Year Book of Orthopedics and Traumatic Surgery, 1954-1955. Edited by EDWARD L. COMPERE, M.D., F.A.C.S., F.I.C.S., Professor and Chairman, Department of Bone and Joint Surgery, Northwestern University Medical School; etc. 7½ × 5⅛ in. Pp. 384, with 193 illustrations. 1955. Chicago: Year Book Publishers Inc. (London: Interscience Publishers Ltd.). 45s.

British Surgical Practice. Surgical Progress, 1955. Under the General Editorship of Sir ERNEST ROCK CARLING, LL.D., F.R.C.S., F.R.C.P., F.F.R., Consulting Surgeon, Westminster Hospital; and Sir JAMES PATERSON ROSS, K.C.V.O., M.S., F.R.C.S., F.A.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. 9¾ × 6¾ in. Pp. 387 + viii, with 145 illustrations. 1955. London: Butterworth & Co. (Publishers) Ltd. 45s.

New Concepts of Surgery of the Vascular System. By EMILE HOLMAN, M.D., Professor of Surgery, Stanford University School of Medicine, San Francisco, Cal. No. 27, *American Lecture Series.* 8½ × 5½ in. Pp. 108 + vi, with 47 illustrations. 1955. Springfield, Ill.: C. C. Thomas (Oxford: Blackwell Scientific Publications). 18s.

Blood Supply and Anatomy of the Upper Abdominal Organs. With a Descriptive Atlas. By NICHOLAS A. MICHELS, M.A., D.Sc., Professor of Anatomy, Jefferson Medical College, Philadelphia. 10 × 7 in. Pp. 581 + xiv, with 172 illustrations, including 166 in colour. 1955. London: Pitman Medical Publishing Co. Ltd. £8.

The Practitioner's Handbook to the Social Services. By ALFRED H. HAYNES, F.W.I.S. 7¼ × 4⅞ in. Pp. 124 + viii. 1955. Bristol: John Wright & Sons Ltd. 9s. 6d.

A Handbook of Modern Operative Surgery. With Chapters on Instruments, Splints, and Bandaging. By K. DAS, M.B. (Cal.), F.R.C.S. (Eng. & Edin.), Associate Professor of Surgery and Surgeon, R. G. Kar (Carmichael) Medical College Hospitals; etc. Second edition. 9¾ × 6¼ in. Pp. 320 + viii, with 246 illustrations and 14 plates. 1955. Calcutta: Hilton & Co. 40s.

Basic Surgical Skills. A Manual with Appropriate Exercises. By ROBERT TAUBER, M.D., F.A.C.S., Assistant Professor of Gynecology and Obstetrics, The Graduate School of Medicine, University of Pennsylvania; etc. 10¾ × 7¾ in. Pp. 75 + viii, with 51 illustrations. 1955. Philadelphia and London: W. B. Saunders Co. 26s.

Modern Trends in Orthopædics. (Second Series.) Edited by Sir HARRY PLATT, LL.D., M.D., M.S., F.R.C.S., F.A.C.S., President, Royal College of Surgeons of England; Emeritus Professor of Orthopædic Surgery, University of Manchester; etc. 9½ × 6¼ in. Pp. 331 + x, with 226 illustrations. 1956. London: Butterworth & Co.(Publishers) Ltd. 65s.

The Back and Its Disk Syndromes. Including Injuries, Diseases, Deformities, and Disabilities. With Notes on The Pelvis and Coccyx. By PHILIP LEWIN, M.D., F.A.C.S., F.I.C.S., Professor Emeritus and Formerly Chairman of Orthopædic Surgery, Northwestern University Medical School. Second Edition. 9¼ × 6 in. Pp. 942, with 371 illustrations and 4 coloured plates. 1955. London: Henry Kimpton. £6 15s.

Keratoplasty. By R. TOWNLEY PATON, M.D., F.A.C.S., Surgeon Director, Manhattan Eye, Ear, and Throat Hospital. 10 × 7½ in. Pp. 280 + xvi, with 87 illustrations. 1955. New York and London: McGraw-Hill Publishing Co. Ltd. 214s.

Chirurgie Plastique. By JEAN SÉCAIL, Toulouse. With a Foreword by Professor JACQUES VIRENQUE. 10⅝ × 7½ in. Pp. 886, with 554 illustrations and 27 plates. 1955. Paris: L'Expansion Scientifique Française. 8000 fr.